A 27-year-old woman, gravida 3 para 0 aborta 3, comes to the office for evaluation of fertility difficulties. The patient was started on combined oral contraceptive pills at age 22. She had no periods while using oral contraceptives and was advised that this was normal and of no concern. The patient stopped her contraception a year ago in an attempt to conceive with her husband but still has not menstruated. Her past medical history includes 3 elective first-trimester pregnancy terminations in her late teens. TSH, FSH, LH, prolactin, and quantitative β-hCG are normal. As part of the evaluation for amenorrhea, 10 days of oral medroxyprogesterone is administered. A few days after completing her progesterone course, the patient has moderately heavy bleeding with some cramping. Which of the following endometrial processes caused the bleeding?

A. Apoptosis
B. Dysplasia
C. Granulation
D. Hyperplasia
E. Hypertrophy

Submit

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- ✓ A. Apoptosis (69%)
- B. Dysplasia (0%)
- C. Granulation (3%)
- D. Hyperplasia (19%)
- E. Hypertrophy (6%)

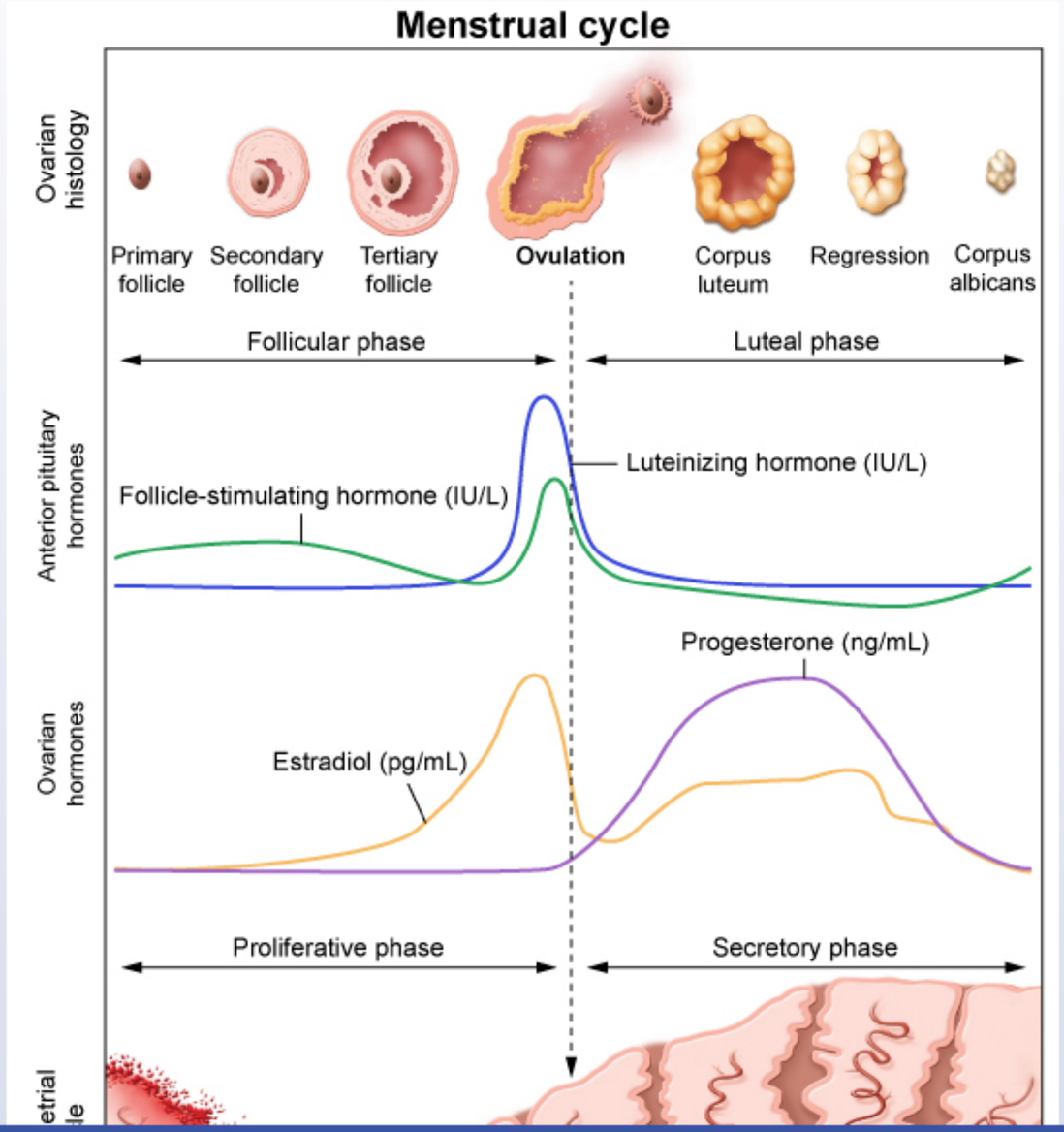
Omitted
Correct answer
A

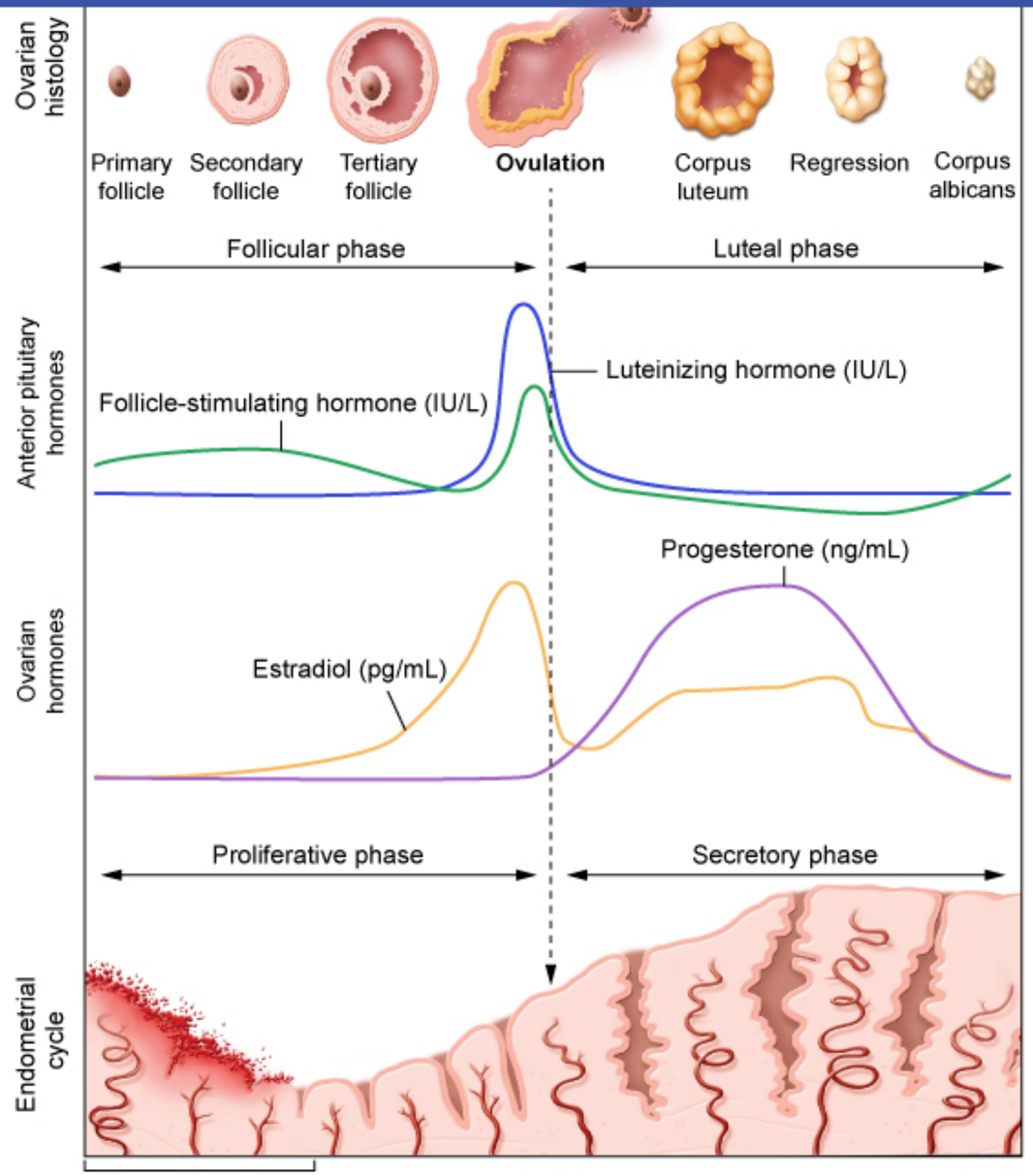
69%
Answered correctly

24 secs
Time Spent

02/17/2020
Last Updated

Explanation


Menstrual cycle
Ovarian histology
Primary follicle
Secondary follicle
Tertiary follicle
Ovulation
Corpus luteum
Regression
Corpus albicans
Follicular phase
Luteal phase
Anterior pituitary hormones
Luteinizing hormone (IU/L)
Follicle-stimulating hormone (IU/L)
Ovarian hormones
Progesterone (ng/mL)
Estradiol (pg/mL)
Proliferative phase
Secretory phase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Anterior pituitary hormones
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Ovarian hormones
Progesterone (ng/mL)
Estradiol (pg/mL)
Proliferative phase
Secretory phase
Endometrial cycle

Day 1 Menses Day 14 Day 28
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Progesterone is typically secreted in the luteal phase of the menstrual cycle and stimulates the endometrium to transform from proliferative to secretory to become a hospitable environment for embryonic implantation. Endometrial glands become more elaborate and the spiral arteries coil. Exogenous intake of progesterone for approximately 10 days similarly matures the endometrial lining.

When the endometrium is no longer exposed to progesterone (eg, in a **progesterone withdrawal** test), prostaglandin production increases, leading to **vasoconstriction of the spiral arteries**. Progesterone withdrawal also causes increased secretion of metalloproteases by endometrial stromal cells (causing degradation of the extracellular matrix) and **apoptosis** of the endometrial epithelium. The net effect is degeneration of the functionalis layer, which sloughs away as **menstrual flow**.

(Choice B) Dysplasia is the abnormal growth of cells, tissues, or organs. In epithelial tissues such as the transformation zone of the cervix, dysplasia is a very early form of precancer.

(Choice C) Granulation is a process of scar formation that involves deposition of connective tissue and angiogenesis. This patient's prior terminations put her at risk for Asherman syndrome and amenorrhea caused by post-procedural intrauterine scarring. Patients with Asherman syndrome do not experience progesterone withdrawal bleeding as the endometrium is essentially replaced with scar tissue.

(Choice D) Hyperplasia is the enlargement of tissue or an organ due to an increase in the number of cells. In the uterus, hyperplasia is frequently a precancerous state caused by excess estrogen exposure that stimulates endometrial proliferation. The progesterone in the patient's combined oral contraceptives and medroxyprogesterone would have suppressed endometrial proliferation.

(Choice E) Hypertrophy is an enlargement of tissue or an organ due to an increase in the size of its cells. Uterine hypertrophy is commonly seen in adenomyosis.

Educational objective:
Progesterone is the primary hormone responsible for stimulating the endometrium so that it is suitable for implantation. Progesterone withdrawal causes endometrial cells to undergo apoptosis, resulting in menstrual bleeding.

References

- Apoptosis in human endometrium and endometriosis.

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References

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Physiology	Female Reproductive System & Breast	Apoptosis
Subject	System	Topic

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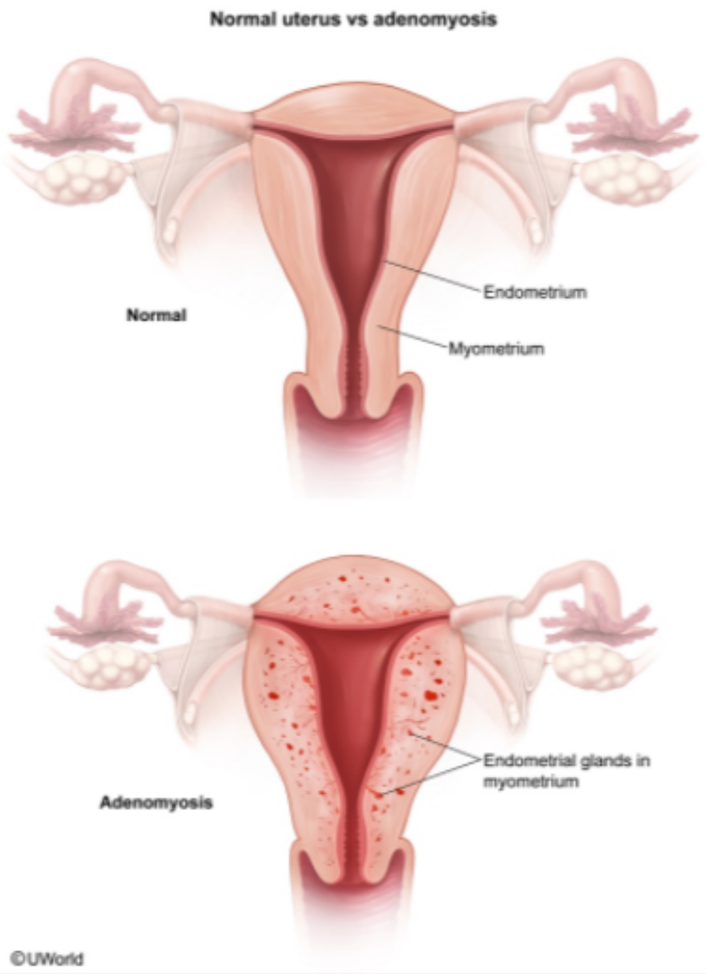
Exhibit Display



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A 34-year-old woman with polycystic ovary syndrome comes to the office with her husband for treatment of infertility. The patient has been unable to conceive despite having unprotected sexual intercourse several times a week for the past 2 years. Her menses are irregular and occur every 2-3 months, consistent with chronic anovulation. She does not use tobacco, alcohol, or illicit drugs. The patient takes no medications and has no allergies. BMI is 32 kg/m^2. Physical examination shows coarse hair on her chin and abdomen. The patient is initially prescribed clomiphene therapy but fails to conceive. She then receives ovulation induction therapy with a short course of menotropins followed by a single injection of human chorionic gonadotropin (hCG). The use of hCG therapy primarily mimics which of the following physiologic events?

- A. Estrogen surge
- B. FSH surge
- C. LH surge
- D. Progesterone surge
- E. Prolactin surge

Submit

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- A. Estrogen surge (3%)
- B. FSH surge (4%)
- ✓ C. LH surge (64%)
- D. Progesterone surge (26%)
- E. Prolactin surge (0%)

Omitted
Correct answer
C

64%
Answered correctly

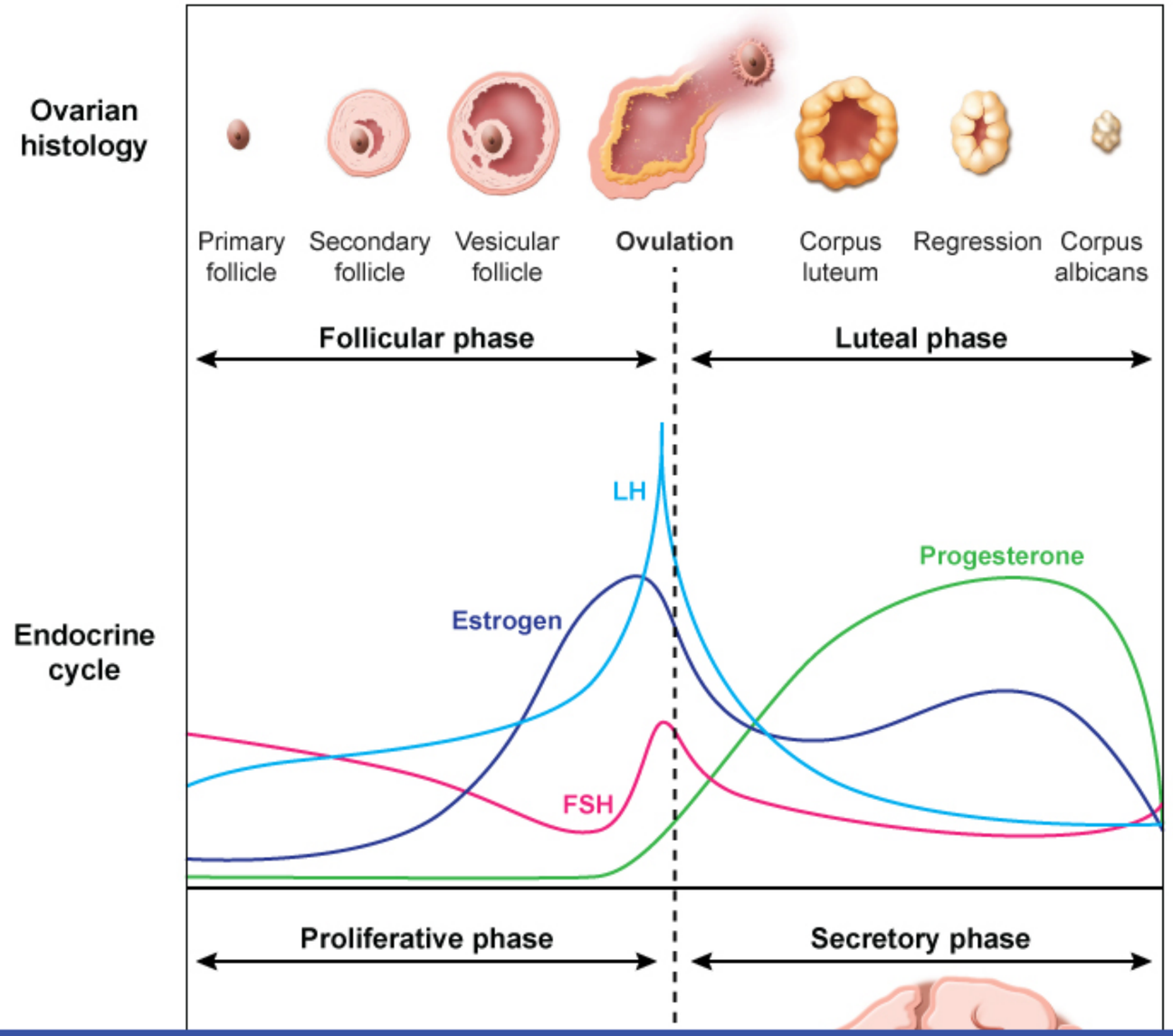
02 secs
Time Spent

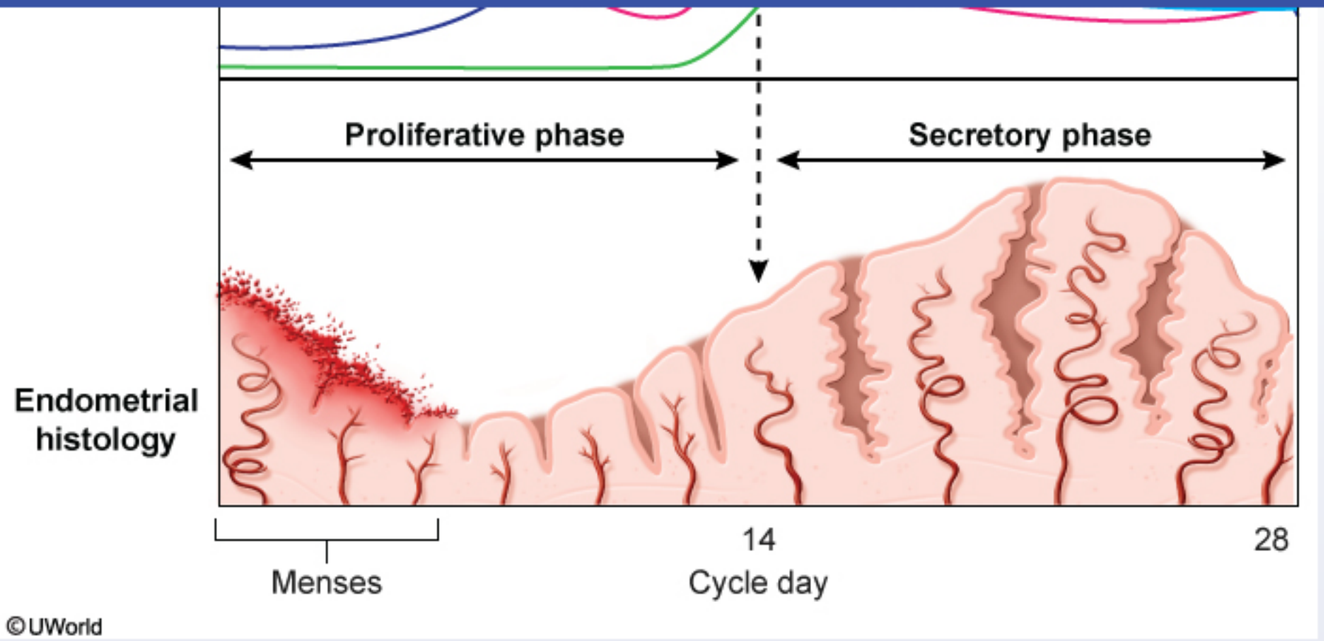
06/12/2020
Last Updated

Explanation

Menstrual cycle

Menstrual cycle





Women of reproductive age experience cyclic hormonal changes of the hypothalamus-pituitary-ovarian axis that normally manifest as monthly ovulation and menstrual bleeding. Pulsatile gonadotropin-releasing hormone from the hypothalamus causes intermittent secretion of FSH and LH from the pituitary. FSH and LH are responsible for the development of the ovarian follicle and ovulation, respectively.

The normal menstrual cycle consists of the follicular and luteal phases. Following the onset of menstruation, FSH stimulates one or more dominant follicles to form in one of the ovaries (follicular phase). FSH also stimulates estrogen production from the ovaries. As the follicular phase advances, a progressive rise in serum estradiol is seen. High estrogen levels in the late follicular phase have a positive feedback effect on LH production, resulting in an LH surge. Ultimately, the **LH surge** causes the rupture of the dominant follicle, leading to extrusion of an ovum (ovulation).

Failure of ovulation (eg, anovulation in polycystic ovary syndrome) is a common cause of infertility. Treatment options include the administration of drugs that act like FSH and LH. Menotropin (human menopausal gonadotrophin) therapy mimics FSH and triggers the formation of a dominant ovarian follicle. When the follicle appears mature, exogenous **human chorionic gonadotropin (hCG)** is administered. The alpha subunit of hCG is structurally similar to LH and therefore simulates the LH surge by **inducing ovulation**.

(ovulation).

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(Choice A) Estrogen levels continue to increase progressively during the follicular phase. Peak estrogen levels are seen just before the LH surge.

(Choice B) The effect of hCG therapy is analogous to the LH surge. Menotropin therapy mimics the FSH surge, which is very small compared to the large LH surge.

(Choice D) Progesterone secretion increases following ovulation with the formation of the corpus luteum. Peak progesterone levels are seen in the mid-luteal phase.

(Choice E) Prolactin increases substantially during pregnancy and peaks at delivery to prepare the breast for lactation. Elevated prolactin levels lead to anovulation (eg, lactational amenorrhea).

Educational objective:
Anovulation is a common cause of infertility. Menotropin (human menopausal gonadotropin) is a treatment option that acts like FSH and triggers the formation of a dominant ovarian follicle. Ovulation is then induced by administration of human chorionic gonadotropin, which mimics the LH surge.

References

- Ovulation triggers in anovulatory women undergoing ovulation induction.

Physiology	Female Reproductive System & Breast	Infertility
Subject	System	Topic

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A 50-year-old woman comes to the office concerned that her menstrual periods have stopped. She took oral contraceptive pills for the past 17 years, which she discontinued 3 months ago, and her menses have not returned. The patient had one spontaneous abortion at age 27 and otherwise has never been pregnant. She is monogamous with her husband, and they have sexual intercourse regularly. The patient has some vaginal dryness but no pain or discomfort with intercourse. BMI is 21 kg/m^2 and vital signs are normal. Speculum examination shows a normal vaginal mucosa and cervix. Bimanual examination shows a normal uterus and ovaries. Urine pregnancy test is negative. Which of the following hormones is most likely elevated in this patient?

A. β-hCG
B. Estradiol
C. FSH
D. Progesterone
E. Prolactin

Submit

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A. β-hCG (0%)
B. Estradiol (5%)
✓ C. FSH (74%)
D. Progesterone (11%)
E. Prolactin (7%)

Omitted
Correct answer
C

74%
Answered correctly

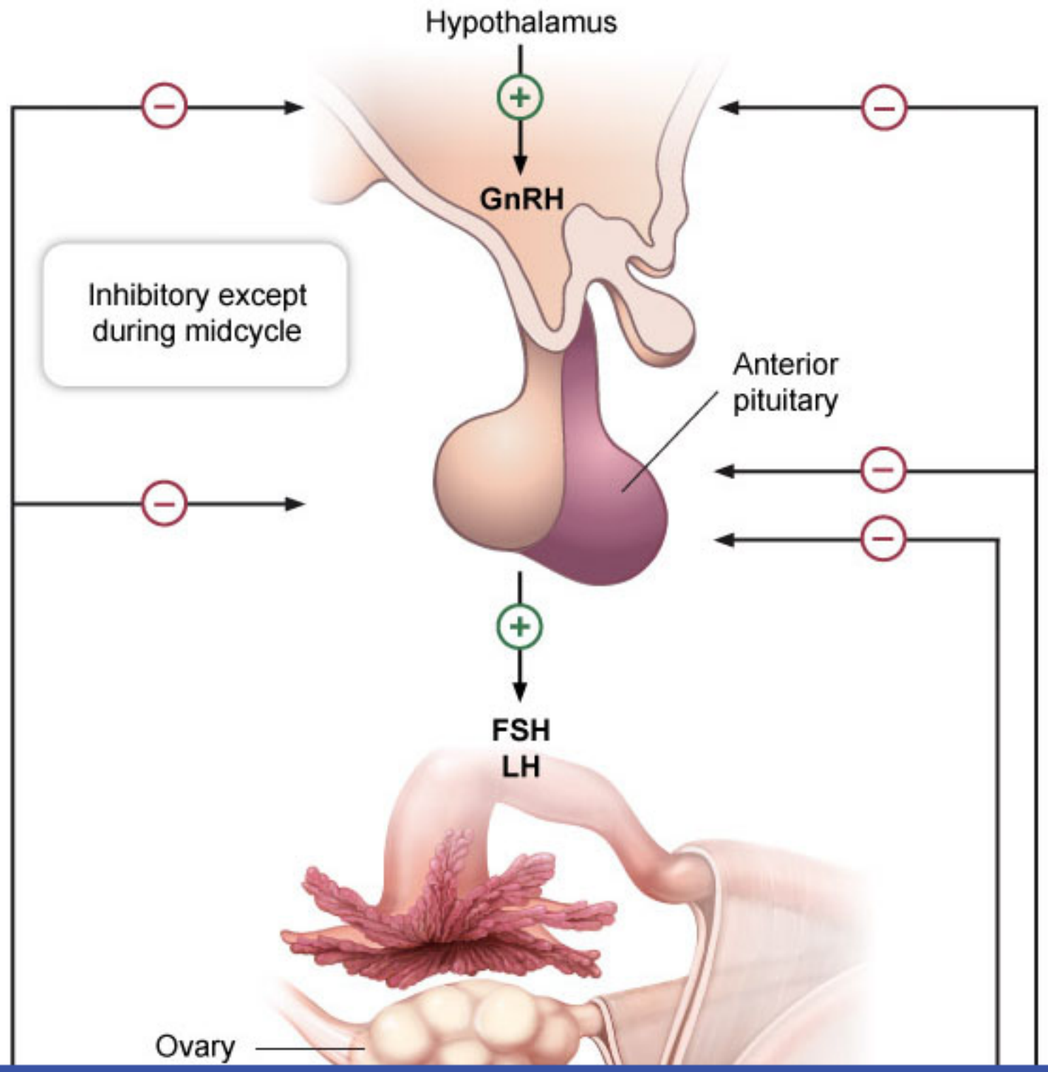
02 secs
Time Spent

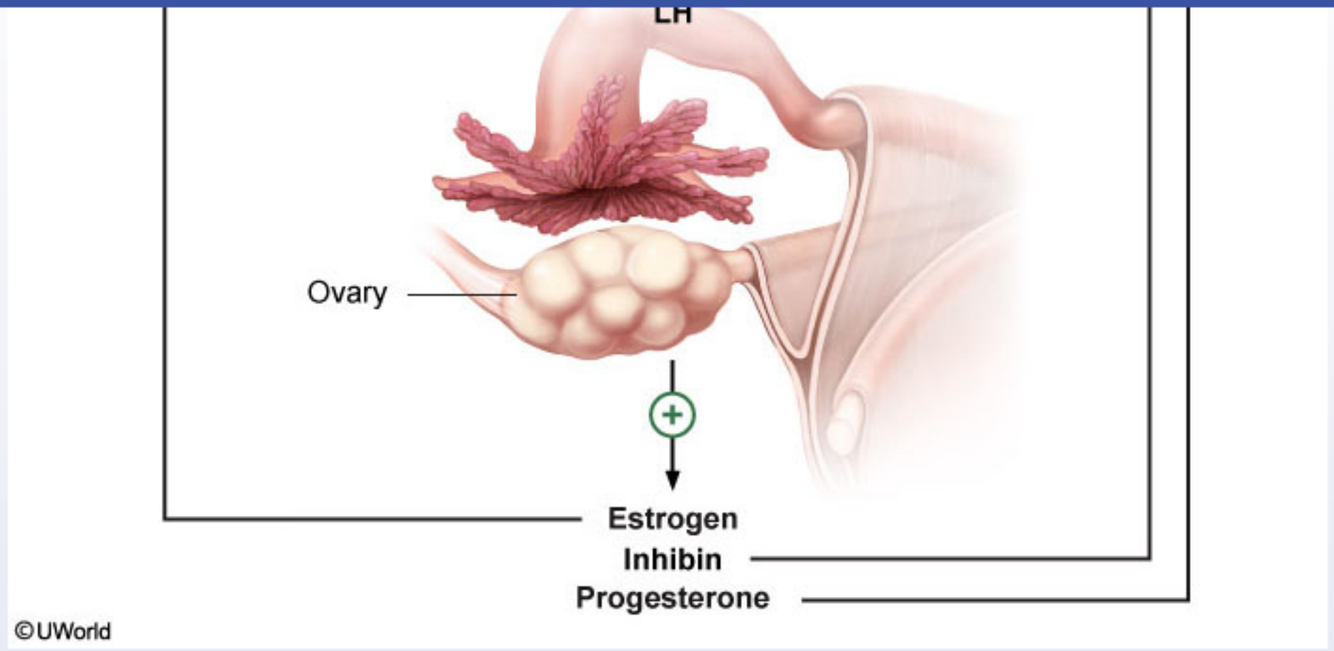
05/11/2020
Last Updated

Explanation

Hypothalamic-pituitary-ovarian axis

Hypothalamus


Hypothalamic-pituitary-ovarian axis
Hypothalamus
GnRH
Inhibitory except during midcycle
Anterior pituitary
FSH
LH
Ovary



Menopause is defined by the permanent cessation of menses for **12 months** and is a normal event of aging caused by exhaustion of ovarian follicles. The mean age of menopause in the United States is 51. Ovarian failure before age 35 is considered premature. During the menopausal transition, **FSH levels increase** due to resistant ovarian follicles and lack of feedback from inhibin. Absence of menstrual cycles with associated **hypoestrogenic symptoms** (eg, hot flashes, vaginal dryness) is highly suggestive of menopause. Menopause is typically diagnosed clinically. However, if the diagnosis is unclear, an elevated serum FSH level can be used for diagnosis as it is a reliable early indicator.

Cyclic and continuous oral contraceptive (OC) regimens are not associated with irregular menses or amenorrhea, and premenopausal patients who stop taking OCs should expect spontaneous return of menses. This patient's age and vaginal dryness make menopausal transition the most likely cause of amenorrhea. OCs may mask vasomotor symptoms that are typical of menopausal transition, and the patient was likely having iatrogenic withdrawal bleeding.

(Choice A) A urine pregnancy test should be performed for any female of reproductive age with amenorrhea. A negative test is a reliable indicator that the patient is not pregnant. Serum β-hCG testing is indicated in cases when the absolute value of the β-hCG would aid in diagnosis and treatment, such as in ectopic or molar pregnancies.

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(Choices B and D) Estradiol and progesterone levels gradually decrease during the menopausal transition due to decreasing ovarian function. Serum estradiol measurement is not a reliable indicator of menopause due to typical fluctuations and gradual decline. After menopause, estrone is produced outside the ovaries and replaces estradiol as the predominant circulating estrogen.

(Choice E) Serum prolactin levels are much less significantly changed during menopause than are FSH levels. Amenorrhea due to a prolactinoma would be diagnosed by detecting an elevated prolactin level. Additional symptoms can include galactorrhea and headache, which this patient does not have.

Educational objective:
Menopause occurs on average at age 51 and is diagnosable retrospectively after 12 months of amenorrhea. An elevated serum FSH level confirms the diagnosis.

References

- ACOG Practice Bulletin No. 14: management of menopausal symptoms.

A patient is treated with a gonadotropin-releasing hormone (GnRH) infusion. An intravenous line is placed and connected to a reservoir through a computerized pump. The pump is programmed to deliver a predetermined dose of GnRH every 90 minutes, which results in a sharp rise in serum GnRH levels with each dose, followed by a rapid return to baseline. LH and FSH levels are monitored in the initial phase of treatment. Which of the following is the most likely indication for using this GnRH infusion?

A. Breast cancer

B. Endometriosis

C. Infertility

D. Precocious puberty

E. Prostate cancer

Submit

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A. Breast cancer (0%)
B. Endometriosis (1%)
✓ C. Infertility (87%)
D. Precocious puberty (4%)
E. Prostate cancer (4%)

Omitted
Correct answer
C

87%
Answered correctly

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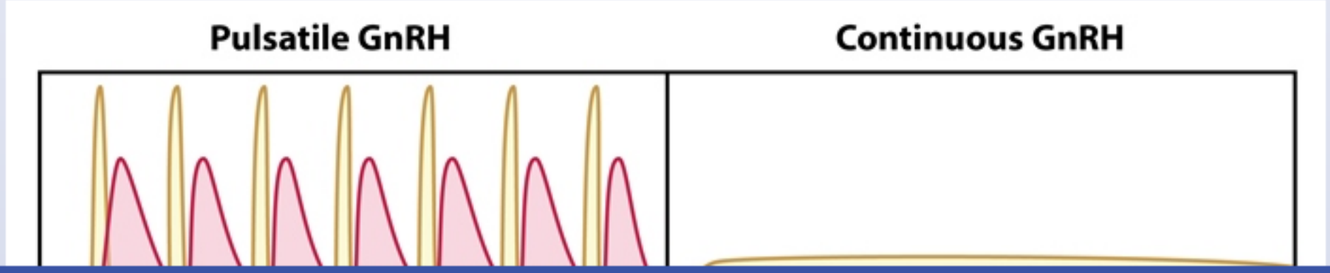
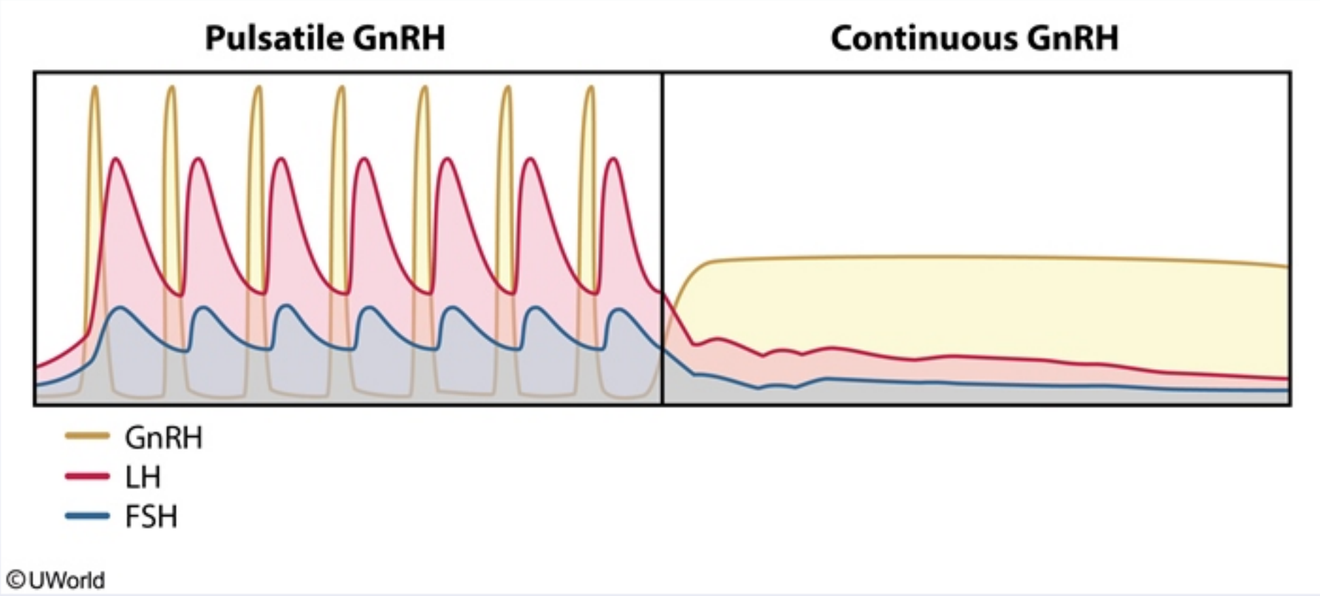
Time Spent

02/08/2020
Last Updated

Explanation





Gonadotropin-releasing hormone (GnRH) is a polypeptide that is normally released from the anterior hypothalamus in a pulsatile manner. GnRH is carried to the anterior pituitary via the portal circulation, where it stimulates FSH and LH production. **Pulsatile** stimulation of pituitary gonadotrophin cells by GnRH leads to upregulation of GnRH receptors and enhanced FSH and LH secretion. FSH and LH are responsible for development of the dominant follicle in the ovaries. Optimal frequency and amplitude of GnRH pulses are crucial for FSH and LH release and subsequent ovulation.

Anovulation due to hypogonadotropic hypogonadism is a common form of **infertility** that can be treated by pulsatile administration of GnRH. GnRH has a very short half-life and is given by a programmable pump that delivers a predetermined dose at physiologic intervals. Ovulation occurs in most patients in 10-20 days. Signs of ovulation include loss of a dominant follicle on ultrasound, surge in urine LH levels, rise in serum progesterone levels, and rise in basal body temperature.

(Choices A, B, D, and E) Constant, rather than pulsatile, GnRH activity causes down-regulation of the GnRH receptors on pituitary gonadotrophin cells, which suppresses LH and FSH secretion. Although it is possible to use a pump to administer GnRH at a steady rate, it has a very short half-life, and long-acting GnRH analogs (eg, leuprolide) are easier to use and can be given monthly by intramuscular injection. Long-

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(Choices A, B, D, and E) Constant, rather than pulsatile, GnRH activity causes down-regulation of the GnRH receptors on pituitary gonadotrophin cells, which suppresses LH and FSH secretion. Although it is possible to use a pump to administer GnRH at a steady rate, it has a very short half-life, and long-acting GnRH analogs (eg, leuprolide) are easier to use and can be given monthly by intramuscular injection. Long-acting GnRH analog therapy is used when suppression of gonadal function is desired, such as in certain patients with prostate cancer, endometriosis, precocious puberty, or premenopausal breast cancer.

Educational objective:
Pulsatile administration of gonadotropin-releasing hormone (GnRH) stimulates FSH and LH release and is useful for the treatment of infertility. Nonpulsatile (constant) infusion of GnRH, or a long-acting analog, suppresses FSH and LH release and subsequently suppresses gonadal function.

References

- Use of gonadotropin-releasing hormone agonists to trigger ovulation.

Physiology	Female Reproductive System & Breast	Infertility
Subject	System	Topic

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A 23-year-old woman, gravida 1, para 0, comes to the office for a routine prenatal care visit. She is at 35 weeks gestation and feels well. She reports regular fetal movement and no contractions, loss of fluid, or vaginal bleeding. Pregnancy to date has been uncomplicated and the patient has no underlying medical conditions. She signed up for a clinical trial investigating prolactin. At 34 weeks gestation, she had a serum prolactin level several times higher than what was recorded prior to pregnancy. Which of the following hormones prevents lactation in this patient?

A. β-hCG

B. Insulin

C. LH

D. Progesterone

E. Thyroxine

Submit

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A. β-hCG (11%)
B. Insulin (0%)
C. LH (5%)
✓ D. Progesterone (80%)
E. Thyroxine (3%)

Omitted
Correct answer
D

80%
Answered correctly

02 secs
Time Spent

04/08/2020
Last Updated

Explanation

Progesterone and estrogen promote normal development and maternal breast growth during the prenatal period. In the first trimester of pregnancy, progesterone is secreted by the **corpus luteum** and is crucial to successful implantation. In the second and third trimesters, progesterone is produced by the **placenta** and suppresses FSH and LH though action on the anterior pituitary **(Choice C)**.

Prolactin is a peptide hormone that promotes lactogenesis (ie, maturation of breast alveolar cells) and **milk production**. It is released by the anterior pituitary gland due to stimulation by thyrotropin-releasing hormone (TRH) and increases steadily in circulation as pregnancy progresses. Although lactogenesis may begin during the second trimester, lactation is **suppressed** due to the high **progesterone** levels inhibiting the binding

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(Choice A) β-hCG is secreted by the embryonic syncytiotrophoblast during the first trimester, rising to its highest levels at the ninth week of gestation. β-hCG serves to maintain the corpus luteum until the placenta can assume responsibility for estrogen and progesterone synthesis. By mid-pregnancy, the corpus luteum degenerates and serum β-hCG decreases to a very low level. Therefore, β-hCG is not likely to have a significant effect on lactation during late pregnancy.

(Choices B and E) Thyroxine and insulin contribute to normal gestational mammary gland hypertrophy. Although high dose thyroxine can decrease the production of TRH, this patient has an elevated prolactin level which indicates that TRH production is not suppressed.

Educational objective:
In pregnancy, progesterone is secreted by the corpus luteum and later by the placenta. Although prolactin secretion increases as pregnancy progresses, high progesterone levels inhibit lactation by preventing binding of prolactin to receptors on alveolar cells in the breast.

References

- Prolactin secretion patterns: basic mechanisms and clinical implications for reproduction

Physiology	Pregnancy, Childbirth & Puerperium	Normal pregnancy
Subject	System	Topic

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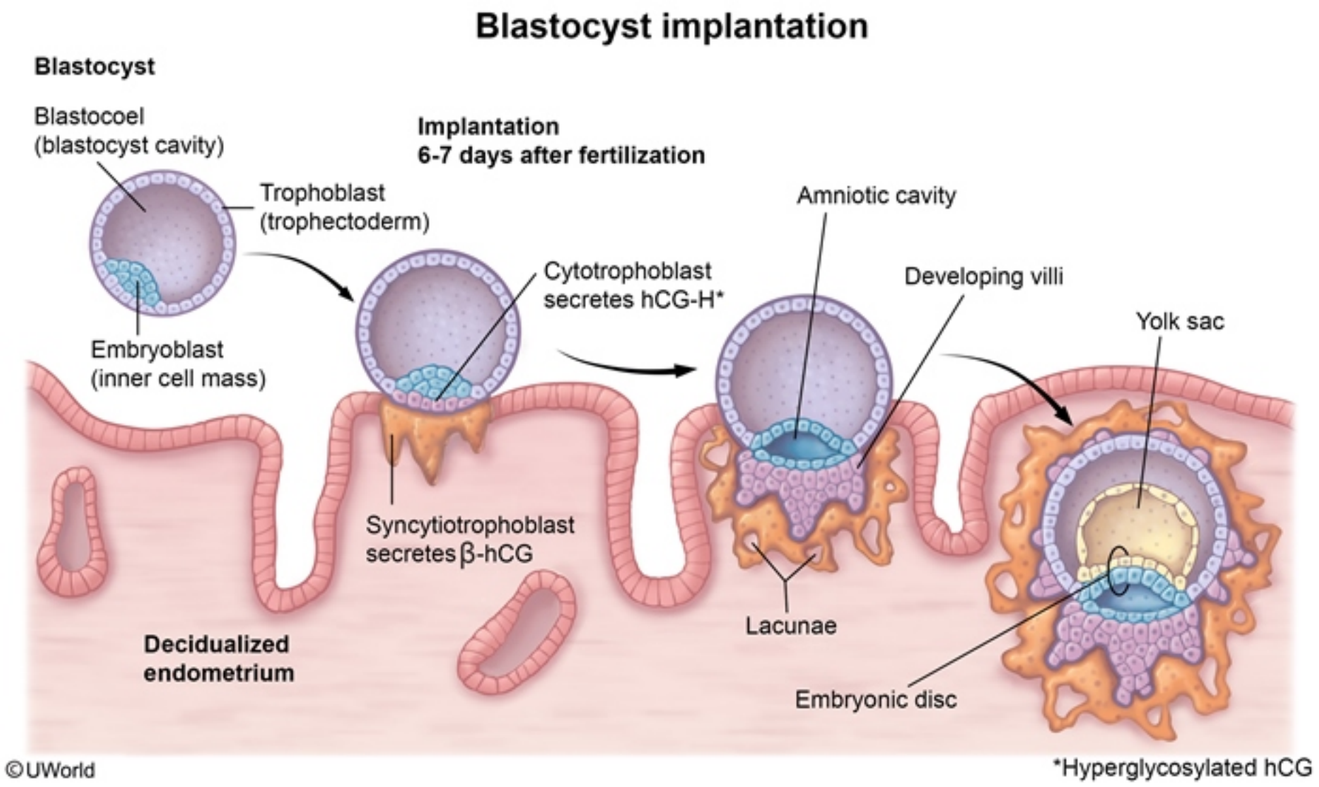
Explanation

Exhibit Display



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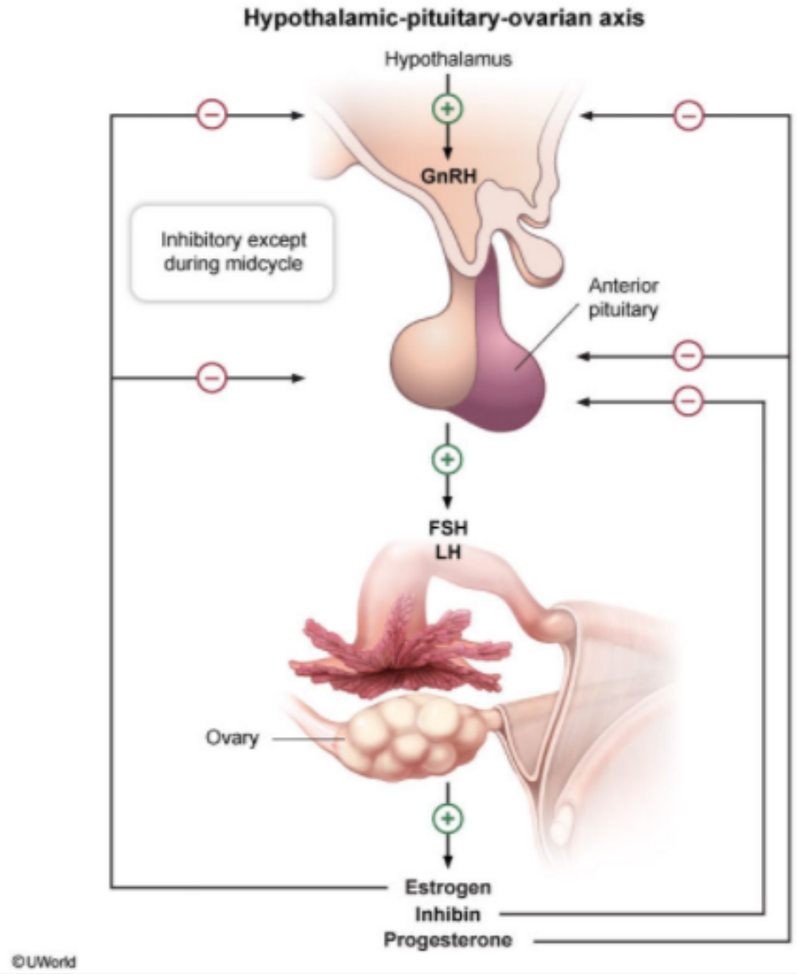
Explanation

Exhibit Display



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A 65-year-old homeless man is brought to the hospital after he is found wandering the streets during a cold winter day. The patient appears confused and has slurred speech. He has no chronic medical conditions and takes no medications. On examination, his temperature is 32 C (89.6 F). Cardiopulmonary examination is normal. No focal neurologic deficits are present. Toxicology screen is negative for any substances. Which of the following physiologic adaptations is most likely occurring in this patient to help maintain homeostasis?

A. Decreased catecholamine release

B. Decreased metabolic rate

C. Decreased muscle tone

D. Increased parasympathetic activity

E. Increased peripheral vasoconstriction

Submit

A 65-year-old homeless man is brought to the hospital after he is found wandering the streets during a cold winter day. The patient appears confused and has slurred speech. He has no chronic medical conditions and takes no medications. On examination, his temperature is 32 C (89.6 F). Cardiopulmonary examination is normal. No focal neurologic deficits are present. Toxicology screen is negative for any substances. Which of the following physiologic adaptations is most likely occurring in this patient to help maintain homeostasis?

- A. Decreased catecholamine release (0%)
- B. Decreased metabolic rate (12%)
- C. Decreased muscle tone (0%)
- D. Increased parasympathetic activity (1%)
- ✓ E. Increased peripheral vasoconstriction (84%)

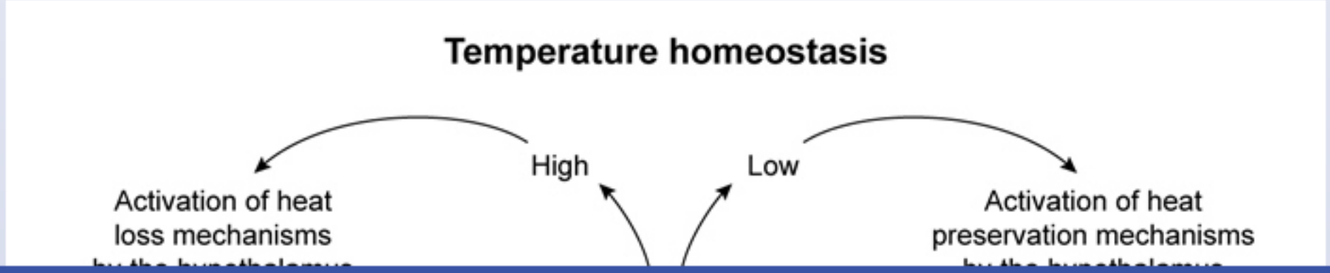
Omitted
Correct answer
E

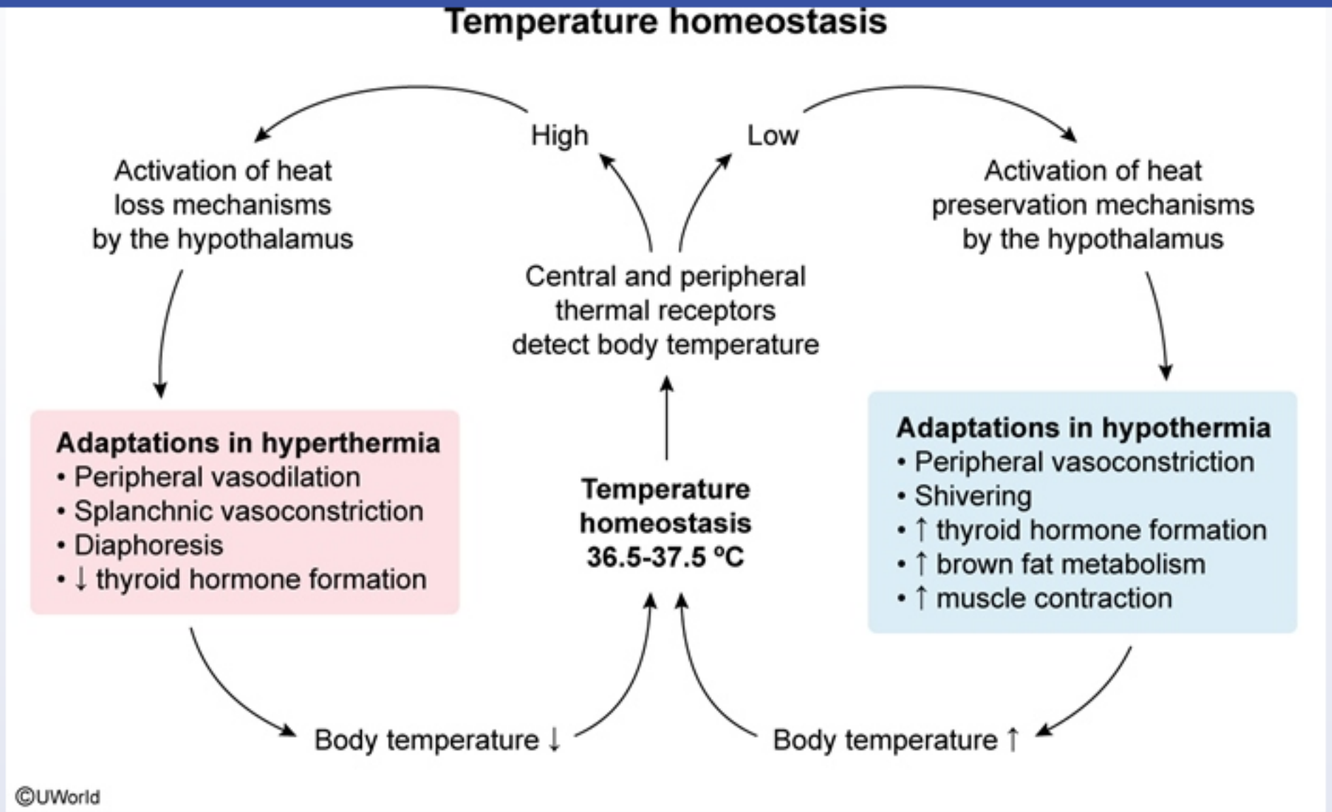
84%
Answered correctly

02 secs
Time Spent

05/26/2020
Last Updated

Explanation





The body maintains its core temperature in a tightly controlled process known as **thermoregulation**. In a normal state, body temperature is maintained between 36.5-37.5 C (97.7-99.5 F) via **anterior hypothalamic control**. Afferent signals (from central and peripheral thermal receptors) are interpreted by the hypothalamus, which promotes temperature homeostasis through alterations in the autonomic nervous system as well as the thyroid and adrenal axes.

Hypothermia, defined as a core body temperature <35 C, occurs when the body loses more heat than it generates. It most commonly occurs due to cold exposure but may also occur due to endocrine disorders (eg, hypothyroidism), skin disorders (eg, burns), abnormal autonomic function (eg, peripheral neuropathies, stroke, spinal cord injury), or drugs that promote vasodilation (eg, alcohol) or impair sympathetic response (eg, beta blockers).

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The following physiologic adaptations occur in patients with hypothermia:

- **Increased sympathetic activity** (catecholamine release): promotes **peripheral vasoconstriction** and results in shunting of blood away from the skin. It also **increases muscle tone** and brown fat metabolism **(Choices A and C)**.
- **Shivering:** rapid involuntary muscle contractions that increase muscle metabolism, generating heat as a byproduct.
- **Increased thyroid function:** prolonged cold exposure leads to increased production of thyroid hormone, which increases basal metabolic rate.

These actions promote normalization of body temperature by reducing heat loss and **increasing metabolic rate** (heat generation) **(Choice B)**.

(Choice D) The sympathetic, not the parasympathetic nervous system, is responsible for the physiologic adaptations in hypothermia. Most blood vessels do not have parasympathetic innervation; therefore, an increase in parasympathetic activity would not have significant effect on vascular tone.

Educational objective:
The hypothalamus controls thermoregulation by promoting alterations in the autonomic nervous system and the adrenal and thyroid axes. Physiologic adaptations in response to hypothermia include increased sympathetic activity and thyroid hormone release, shivering, and peripheral vasoconstriction. These actions normalize body temperature by reducing heat loss and increasing metabolic rate (promoting thermogenesis).

References

- Regulation of body temperature by the nervous system.

A 37-year-old woman, gravida 2 para 1, at 30 weeks gestation comes to the office for a routine prenatal examination. She has no medical problems and takes a daily prenatal vitamin. Her pregnancy has been uncomplicated to date, and fetal movement is present. The patient has no vaginal bleeding, contractions, or loss of fluid. Physical examination shows a uterine size consistent with dates and a fetal heart rate of 160/min. Routine blood work obtained before pregnancy showed no abnormalities. At the last visit, she drank a solution containing 50 g of glucose, and serum glucose was abnormally elevated an hour later. Which of the following hormones is most likely contributing to this patient's abnormal laboratory findings?

A. hCG
B. Human placental lactogen
C. Oxytocin
D. Prolactin
E. Thyroxine

Submit

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A. hCG (13%)
✓ B. Human placental lactogen (70%)
C. Oxytocin (1%)
D. Prolactin (5%)
E. Thyroxine (9%)

Omitted
Correct answer
B

70%
Answered correctly

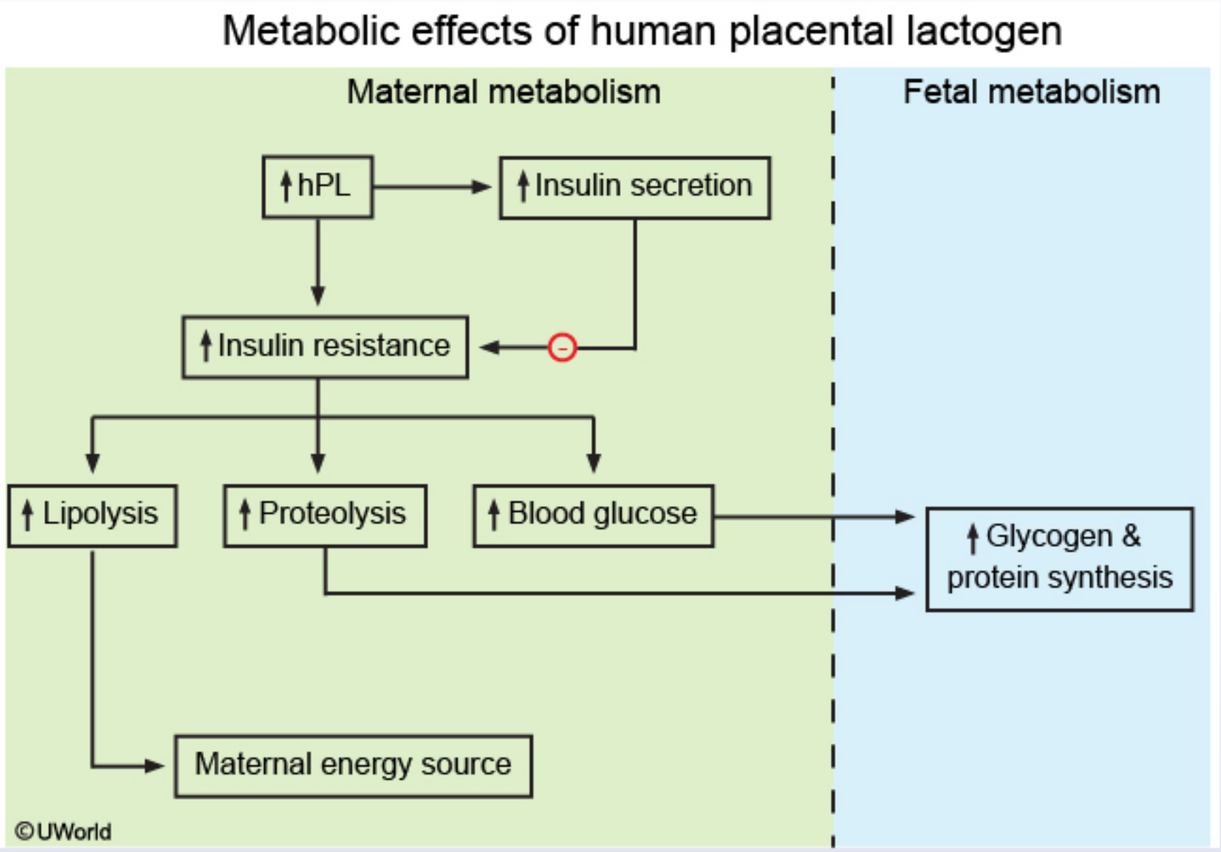
02 secs
Time Spent

07/01/2020
Last Updated

Explanation

Metabolic effects of human placental lactogen

Maternal metabolism	Fetal metabolism



A physiologic increase in maternal **insulin resistance** occurs during the **second and third trimesters** to ensure a readily available supply of glucose and amino acids to the fetus. This increase in insulin resistance is primarily due to the action of **human placental lactogen (hPL)**, a peptide hormone secreted by the syncytiotrophoblast. The rise in insulin resistance leads to **increased glucose levels** in the maternal circulation; glucose freely crosses the placenta and is continuously consumed by the fetus for energy. Maternal lipolysis is also increased by hPL, with the resulting free fatty acids and ketones providing energy to the mother (preserving glucose and amino acids for the fetus). In cases of maternal malnutrition, the increased ketones can also provide the fetus with energy.

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hPL also **stimulates pancreatic beta cell insulin production**. Gestational diabetes mellitus results when pancreatic function is not sufficient to overcome the pregnancy-related increase in insulin resistance. The average levels of hPL rise with increasing gestational age, reflecting the increasing energy requirements of the growing fetus. Screening for **gestational diabetes** is therefore more accurate in the third trimester and can be done with an **oral glucose challenge** and subsequent measurement of serum glucose levels.

(Choice A) In early pregnancy, the placental syncytiotrophoblast secretes human chorionic gonadotropin, a peptide hormone, which stimulates the corpus luteum to produce progesterone, a steroid hormone. Progesterone is necessary to maintain the secretory endometrium, allowing the pregnancy to persist through term.

(Choice C) Oxytocin plays an important role in uterine contraction and the milk letdown reflex, but it does not affect glucose and lipid metabolism.

(Choice D) Prolactin is a peptide hormone secreted by lactotroph cells in the anterior pituitary. Prolactin is responsible for milk production and lactation in postpartum women.

(Choice E) Pregnancy increases the levels of thyroid-binding globulin, leading to increased total circulating T_3 and T_4. However, free thyroid hormone levels remain essentially normal.

Educational objective:
Human placental lactogen increases maternal insulin resistance during the second and third trimesters, leading to a rise in serum glucose that helps provide adequate nutrition to the growing fetus. Gestational diabetes occurs when the compensatory rise in maternal insulin secretion is inadequate to prevent serum glucose levels from reaching excessively high levels.

References

- Gestational diabetes mellitus resulting from impaired beta-cell compensation in the absence of FoxM1, a novel downstream effector of placental lactogen

overcome the pregnancy-related increase in insulin resistance. The average levels of hPL rise with increasing gestational age, reflecting the increasing energy requirements of the growing fetus. Screening for **gestational diabetes** is therefore more accurate in the third trimester and can be done with an **oral glucose challenge** and subsequent measurement of serum glucose levels.

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References

- Gestational diabetes mellitus resulting from impaired beta-cell compensation in the absence of FoxM1, a novel downstream effector of placental lactogen.
- Placental hormones and the control of maternal metabolism and fetal growth.

Physiology	Pregnancy, Childbirth & Puerperium	Gestational diabetes
Subject	System	Topic

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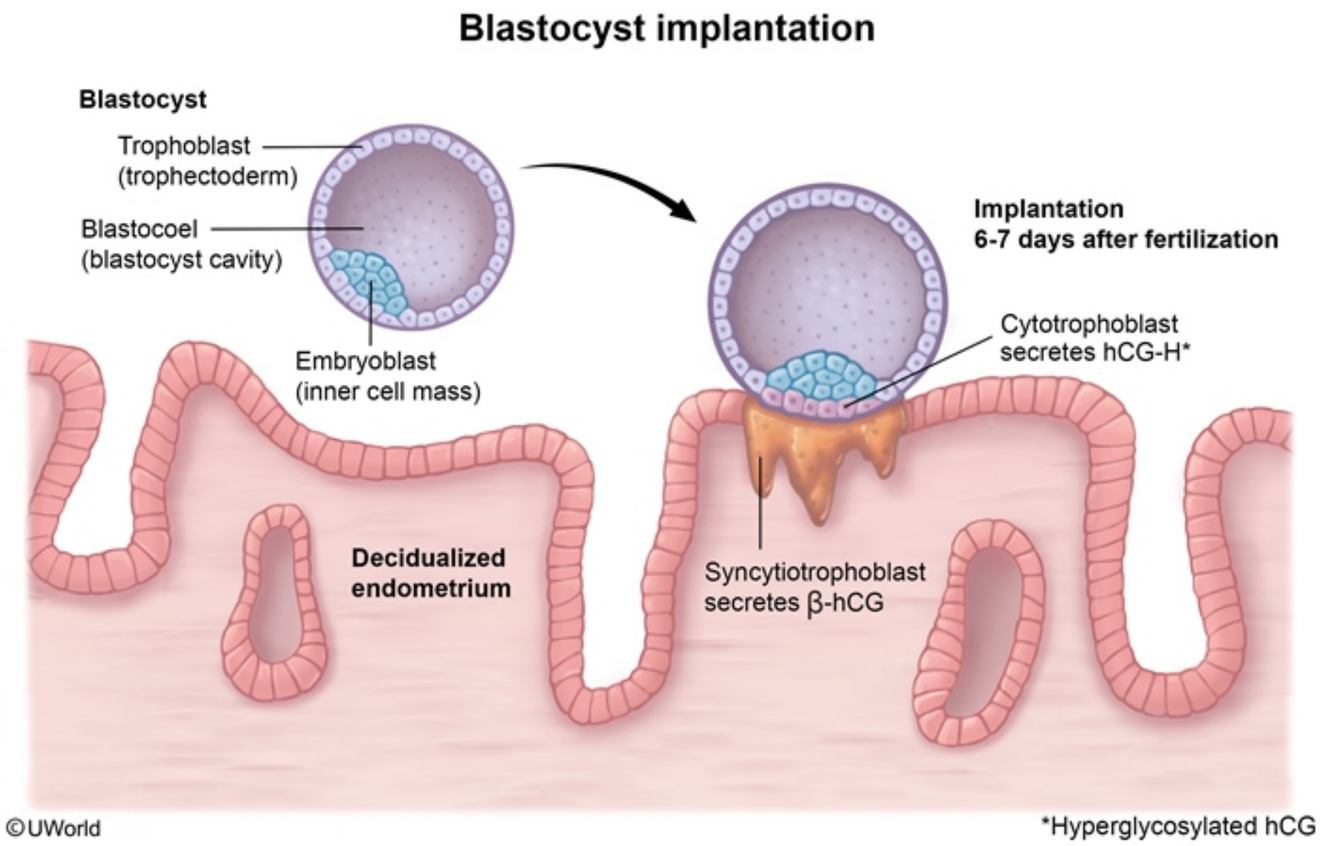
Exhibit Display



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A 28-year-old woman comes to the office for a preconception visit. She has never been pregnant and would like to know how to improve her chances of conceiving. The patient has no family history of genetic abnormalities or infertility. Menarche was at age 13. She menstruates every 28 days, and bleeding lasts for 4 days. She has had no prior surgeries or sexually transmitted infections. Her husband has not fathered a child and has no urogenital problems. The couple has intercourse several times a month. Which of the following hormones would increase the most in concentration after ovulation?

- A. Androstenedione
- B. Estrogen
- C. FSH
- D. GnRH
- E. LH
- F. Progesterone

Submit

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- A. Androstenedione (0%)
- B. Estrogen (2%)
- C. FSH (1%)
- D. GnRH (0%)
- E. LH (5%)
- ✓ F. Progesterone (90%)

Omitted
Correct answer
F

90%
Answered correctly

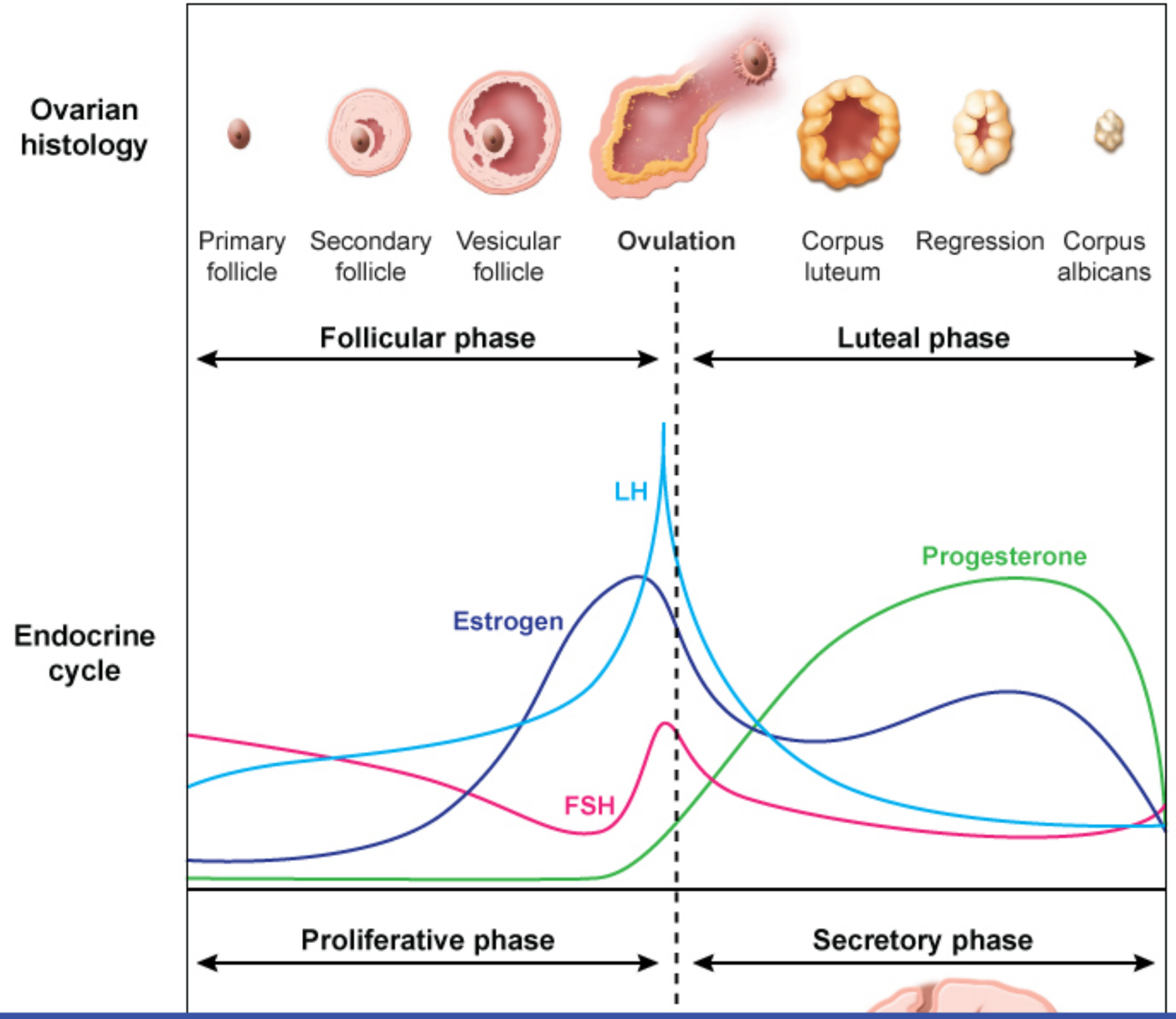
02 secs
Time Spent

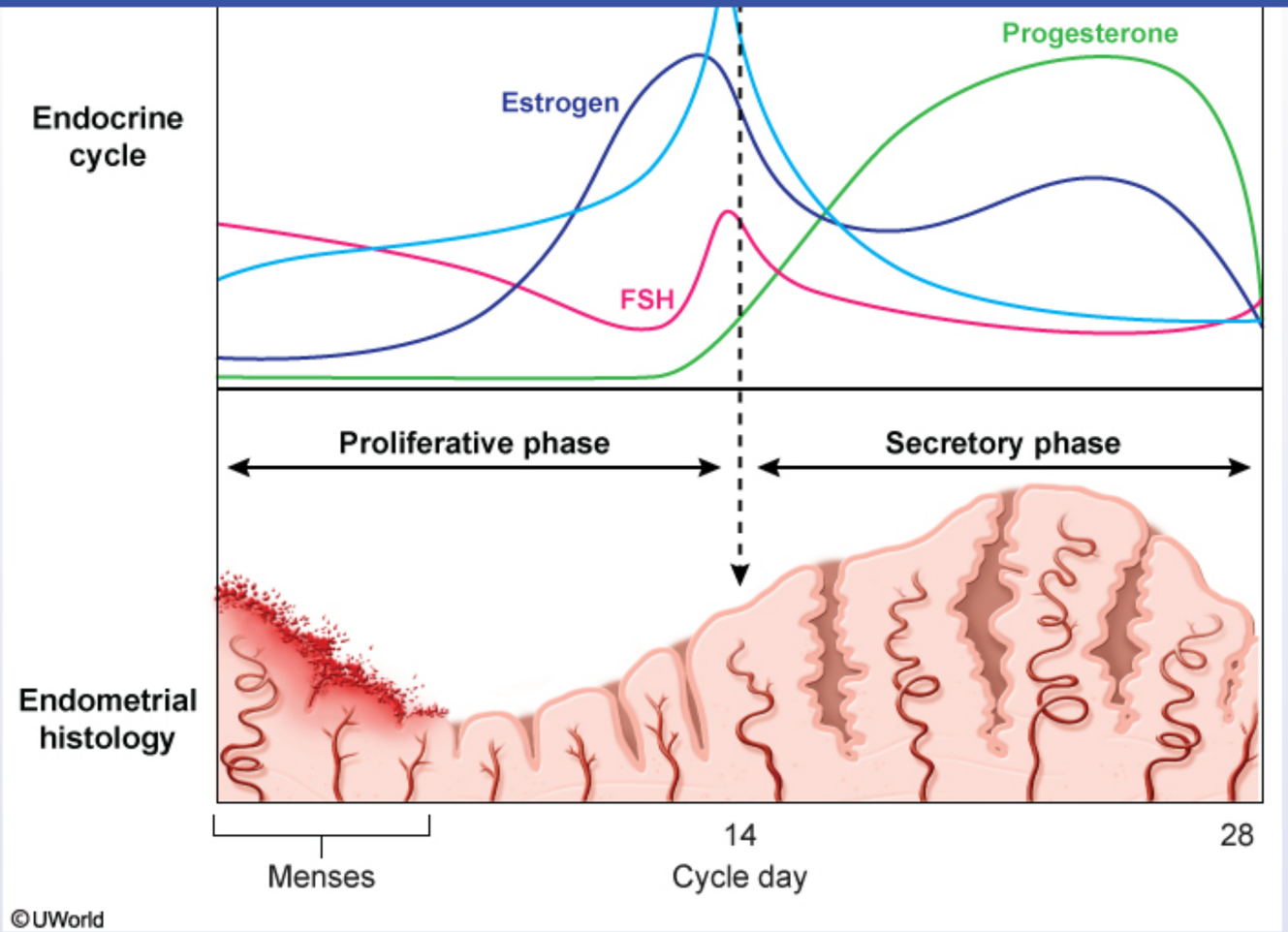
05/05/2020
Last Updated

Explanation

Menstrual cycle

Menstrual cycle





The primary hormones involved in the menstrual cycle are FSH and LH (both from the anterior pituitary) and progesterone and estrogen (both from the ovaries). Many of these names signify their function (eg, progesterone = progestation).

Following the onset of menstruation (day 1), pituitary FSH stimulates the ovary to recruit 1 primary follicle, which becomes the **dominant follicle**. FSH stimulates granulosa cells inside the follicle to produce estrogen, leading to a **progressive rise in serum estrogen**. During the 14-day maturation process (follicular phase of the menstrual cycle), the follicle enlarges and becomes fluid-filled, and the primary oocyte becomes a

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Following ovulation, the granulosa and theca cells of the ovarian follicle luteinize to form the **corpus luteum**; this secretes relatively **high levels of progesterone** and moderate levels of estrogen for the next 14 days (the luteal phase of the menstrual cycle). Progesterone stimulates the endometrium to transform from proliferative to **secretory** to become a hospitable environment for implantation.

(Choice A) Androstenedione is a weak androgen and a precursor to testosterone and estrogen, not progesterone. In women, androstenedione is synthesized from cholesterol in ovarian theca cells and aromatized to estrogen in granulosa cells. Peak serum levels would occur before ovulation.

Education objective:
Of all hormones influencing the menstrual cycle (LH, FSH, estrogen, progesterone), progesterone increases the most in concentration after ovulation. During the latter half of the menstrual cycle, the corpus luteum secretes high levels of progesterone, which thickens the endometrium and prepares it to receive and nourish a blastocyst.

References

- The endocrinology of the menstrual cycle.

Physiology	Female Reproductive System & Breast	Menstrual cycles
Subject	System	Topic

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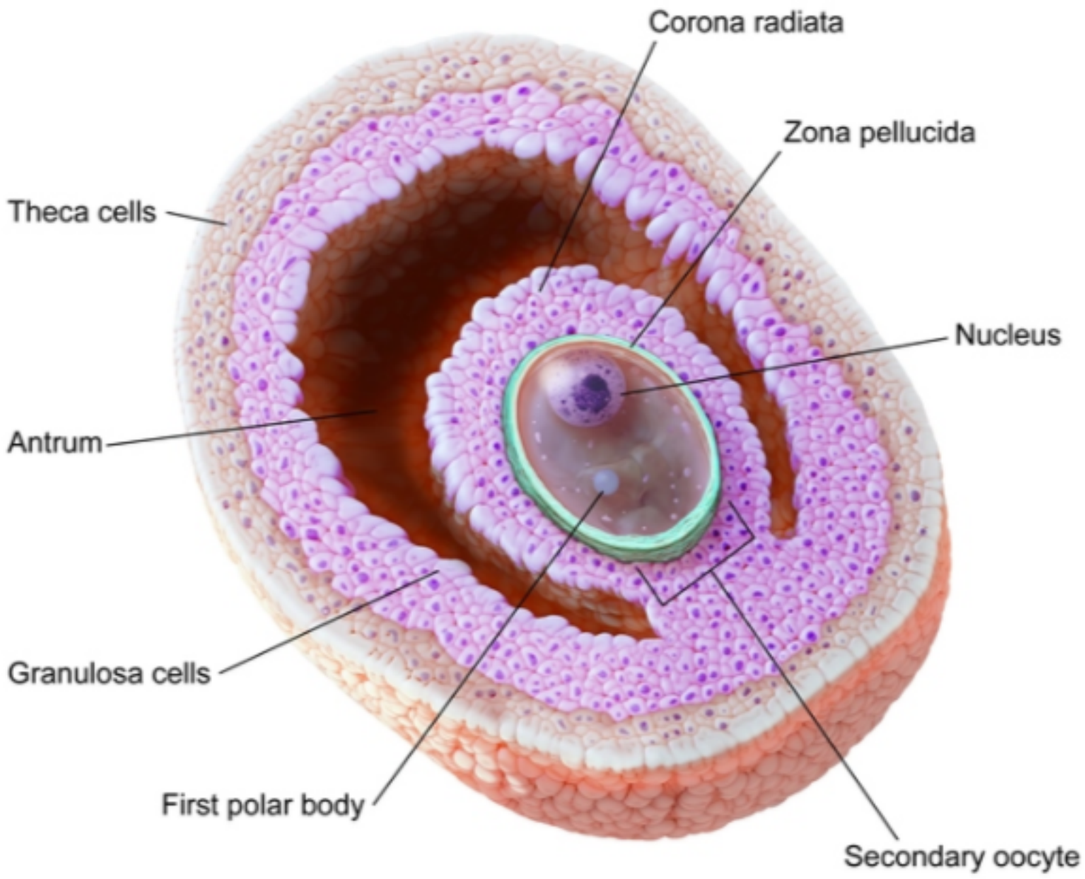
Exhibit Display

Ovarian tertiary follicle



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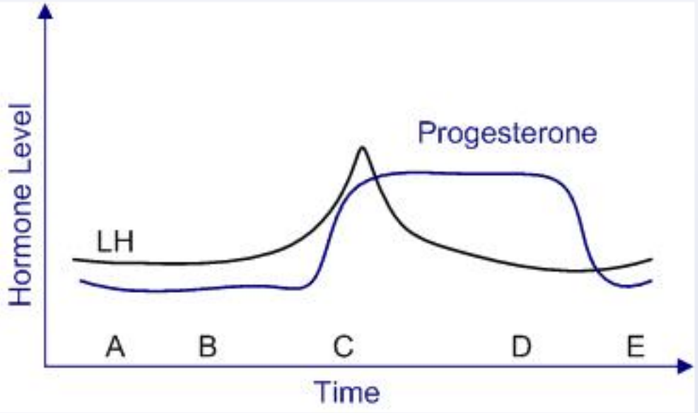
Subject System Topic

A 26-year-old woman, para 0, comes to the office for follow-up of irregular menstrual periods. She has a period every 15-90 days that lasts 2-14 days and ranges from spotting to quarter-sized clots. The patient and her husband have been trying to conceive, but it has been difficult to time intercourse given her erratic menstrual cycles. She has been exercising and losing weight and now has a BMI of 32 kg/m^2. Gynecologic examination shows normal external genitalia, a small mobile uterus, and normal adnexa. Endometrial sampling reveals coiled glands filled with carbohydrate-rich mucus, edematous stroma, and tortuous spiral arteries. At which time point on the graph below was the endometrial sampling most likely obtained?



A. A
B. B
C. C
D. D
E. E

Submit

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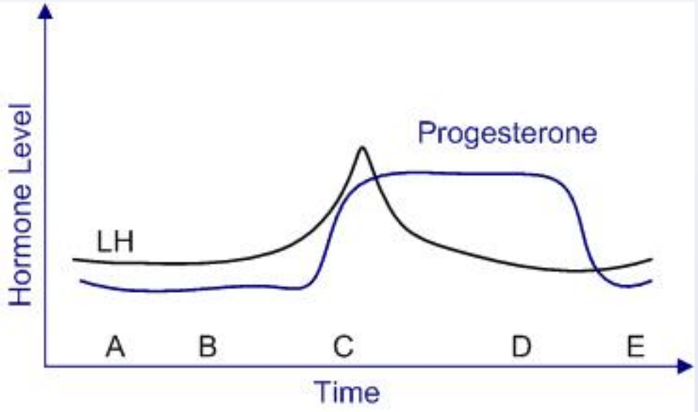
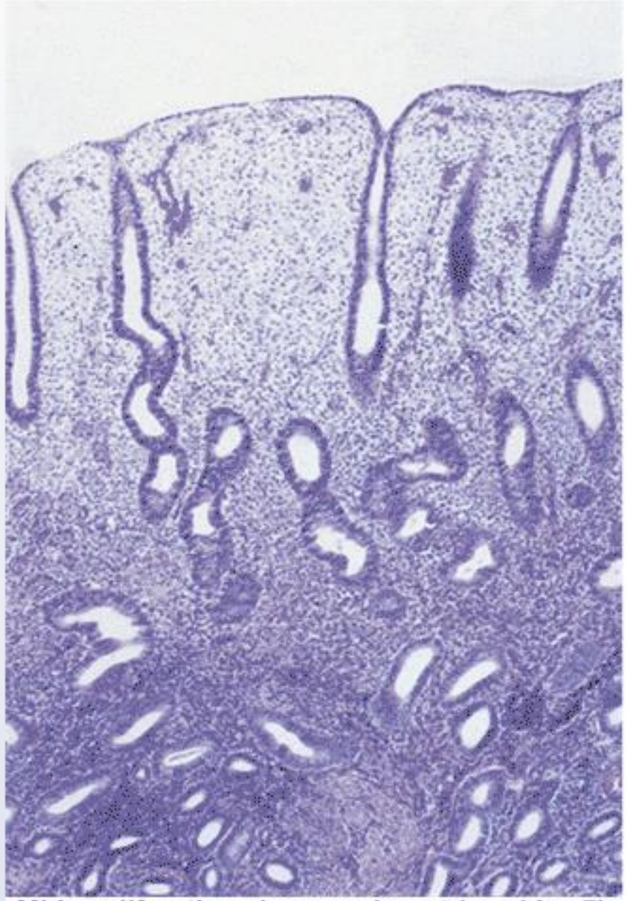
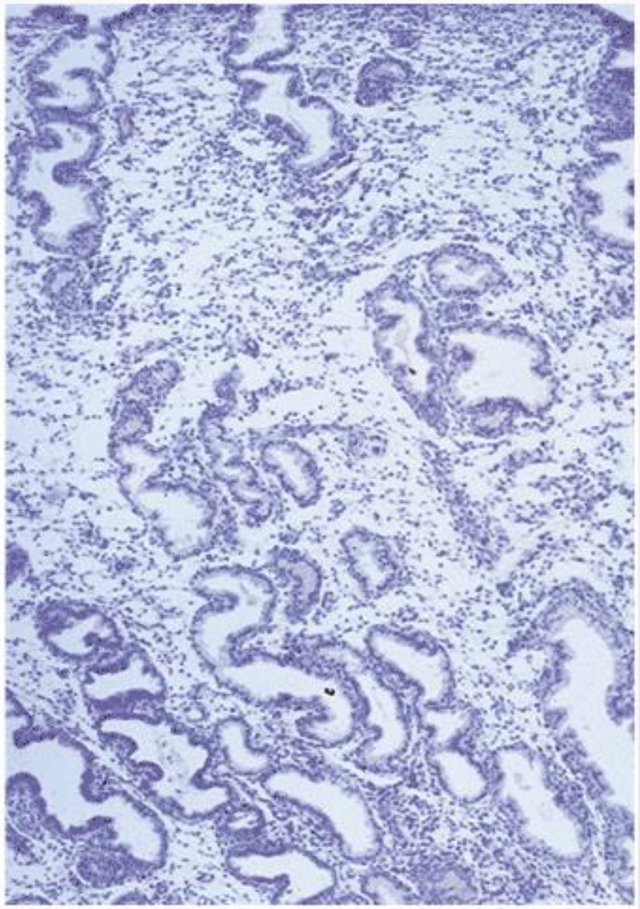


A. A (0%)
B. B (2%)
C. C (12%)
✓ D. D (82%)
E. E (1%)

Omitted



Mid-proliferative phase endometrium (day 7). The endometrium demonstrates uniform development, with a gland:stroma ratio of less than 1:1. The glands are straight and narrow, and contain small lumens.



Mid-secretory phase endometrium (day 21). The gland:stroma ratio has increased to approximately 1:1 because the amplified stromal volume is associated with marked stromal edema. The glands are dilated and coiled, and contain wide lumens.

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The uterine **endometrium** is a highly specialized mucosa that undergoes histologic transformation during the menstrual cycle in preparation for

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The uterine **endometrium** is a highly specialized mucosa that undergoes histologic transformation during the menstrual cycle in preparation for zygote implantation. The upper layer of the endometrium (the stratum functionale) consists of lamina propria studded with tubular glands, spiral arteries, and dilated capillaries. Histologic examination of these components with an endometrial biopsy allows for endometrial dating and evaluation for pathological processes.

A normal menstrual cycle lasts for 21-35 days (28+/-7 days). The **proliferative phase** is the first half of the menstrual cycle (**days 1-14**), beginning with the first day of menses and ending with ovulation. During this time, estrogen stimulates proliferation of the stratum functionale. Normal proliferative endometrium consists of nonbranching, nonbudding, uniform glands evenly distributed throughout a uniform stroma **(Choices A and E)**. In the midproliferative phase **(Choice B)**, the glands are tubular, narrow, and lined with pseudostratified, elongated, mitotically active epithelial cells. The stratum functionale contains compact, nonedematous stroma. The uterine glands have increased in length and girth but still remain relatively straight. No secretions are present in the glandular lumens. The endometrium thickens, but the coiled spiral arteries remain limited to the deeper layers. At the end of the proliferative phase, ovulation occurs. Endometrial biopsy at ovulation shows a late proliferative endometrium with coiled glands and occasional cytoplasmic vacuoles in the glandular epithelium **(Choice C)**.

The **secretory phase** is the second half of the menstrual cycle (**days 15-28**), which follows ovulation. During this time, progesterone secreted by the corpus luteum in the ovary promotes the development of secretory endometrium. The glands increase in size and become more coiled, and the cells lining the glands acquire large cytoplasmic vacuoles. Glycogen-rich mucus is released into the glandular lumens. The stroma becomes increasingly edematous, and the prominent spiral arteries extend to the endometrial surface. The endometrial biopsy taken in this patient is consistent with the mid-secretory phase.

Educational objective:
The secretory phase of the menstrual cycle occurs between ovulation and menses, from days 15-28 of the normal menstrual cycle. Progesterone released by the corpus luteum causes the uterine glands to coil and secrete glycogen-rich mucus in preparation for embryo implantation. The endometrial stroma becomes edematous and completely traversed by tortuous spiral arteries that extend from the deeper layers to the uterine lumen.

References

- Endometrial biopsy in DUB.

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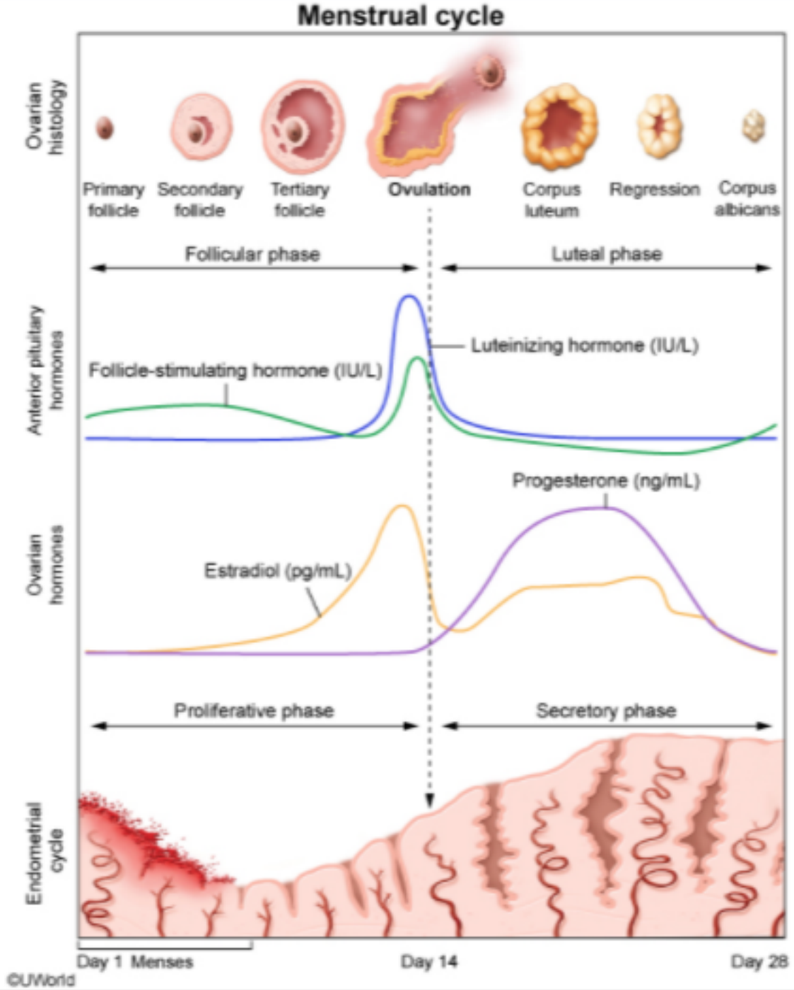
Exhibit Display



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A 30-year-old nulliparous woman comes to the office for evaluation of infertility. She has been attempting to conceive with her partner of 10 years for the past 2 years. Menarche was at age 11, and her menstrual cycles occur 2-3 times per year and last 7-10 days. The patient does not use tobacco, alcohol, or illicit drugs. Her blood pressure is 128/84 mm Hg and pulse is 84/min. BMI is 35 kg/m^2. Physical examination shows mild acne and hair growth on the upper lip and chin. This patient is at greatest risk for which of the following complications?

A. Adrenal atrophy

B. Cushing syndrome

C. Diabetes mellitus, type 1

D. Endometrial carcinoma

E. Vaginal adenosis

Submit

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A. Adrenal atrophy (6%)
B. Cushing syndrome (10%)
C. Diabetes mellitus, type 1 (9%)
✓ D. Endometrial carcinoma (69%)
E. Vaginal adenosis (3%)

Omitted
Correct answer
D

69%
Answered correctly

02 secs
Time Spent

02/23/2020
Last Updated

Explanation

Polycystic ovary syndrome	
Clinical features	• **Androgen excess**: Hirsutism, acne, androgenic alopecia • **Ovarian dysfunction**: Menstrual irregularity, polycystic ovaries • **Insulin resistance**: Acanthosis nigricans, glucose

Polycystic ovary syndrome	
Clinical features	• **Androgen excess**: Hirsutism, acne, androgenic alopecia • **Ovarian dysfunction**: Menstrual irregularity, polycystic ovaries • **Insulin resistance**: Acanthosis nigricans, glucose intolerance/diabetes, metabolic syndrome • **Obesity**
Treatment	• Weight loss • Combination hormonal contraceptives • Metformin (if hyperglycemia/diabetes)

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This patient has **polycystic ovary syndrome (PCOS)**, a condition characterized by at least 2 of the following 3 criteria: signs of **hyperandrogenism**, **irregular periods**, and/or **polycystic ovaries on ultrasound**. PCOS results from increased activity of 17α-hydroxylase; 17,20 lyase; and 3β-hydroxysteroid dehydrogenase. The overexpression of these enzymes results in elevated androgen levels (eg, testosterone, androstenedione, DHEA) and the clinical consequences of hirsutism and acne.

Excess androgen prevents development of a monthly dominant follicle, resulting in **anovulatory** cycles. In turn, menstrual irregularity (most often oligomenorrhea) results in **decreased progesterone** secretion. Progesterone has growth-inhibitory effects on the endometrium and counters estrogen-driven proliferation. The resulting imbalance of estrogen and progesterone places the patient with PCOS at long-term risk for **endometrial hyperplasia** and **adenocarcinoma**. In addition, anovulatory cycles often result in fertility difficulties as seen in this patient.

(Choice A) Autoimmune-mediated destructive adrenal atrophy is the most common cause of Addison disease, which presents as severe fatigue, weight loss, and low blood pressure due to glucocorticoid and mineralocorticoid deficiency. In contrast to PCOS, women may experience axillary and pubic hair loss due to adrenal androgen deficiency.

(Choice B) Patients with Cushing syndrome have symptoms similar to those of patients with PCOS such as obesity, menstrual irregularities, and

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(Choice A) Autoimmune-mediated destructive adrenal atrophy is the most common cause of Addison disease, which presents as severe fatigue, weight loss, and low blood pressure due to glucocorticoid and mineralocorticoid deficiency. In contrast to PCOS, women may experience axillary and pubic hair loss due to adrenal androgen deficiency.

(Choice B) Patients with Cushing syndrome have symptoms similar to those of patients with PCOS such as obesity, menstrual irregularities, and increased body hair. However, hypertension, abdominal striae, and supraclavicular fat pads are also typically seen in Cushing syndrome due to excess cortisol.

(Choice C) PCOS is a risk factor for type 2 diabetes mellitus (T2DM) due to increased insulin resistance. In contrast, patients with a family history of T1DM are at increased risk of developing T1DM, which results from decreased insulin secretion.

(Choice E) Vaginal adenosis is the persistence of glandular columnar epithelium in the vagina and is a precursor for clear cell adenocarcinoma of the vagina. Female offspring exposed to diethylstilbestrol in utero are at increased risk and may present with vaginal discharge or vaginal cysts/fleshy colored lesions.

Educational objective:
Polycystic ovary syndrome (PCOS) is associated with oligomenorrhea, hirsutism, and polycystic ovaries. Disruption in intraovarian steroidogenesis causes anovulatory cycles and results in chronic estrogen stimulation with decreased progesterone secretion, placing PCOS patients at risk for endometrial hyperplasia/carcinoma.

References

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(Choice A) Autoimmune-mediated destructive adrenal atrophy is the most common cause of Addison disease, which presents as severe fatigue, weight loss, and low blood pressure due to glucocorticoid and mineralocorticoid deficiency. In contrast to PCOS, women may experience axillary and pubic hair loss due to adrenal androgen deficiency.

(Choice B) Patients with Cushing syndrome have symptoms similar to those of patients with PCOS such as obesity, menstrual irregularities, and increased body hair. However, hypertension, abdominal striae, and supraclavicular fat pads are also typically seen in Cushing syndrome due to excess cortisol.

(Choice C) PCOS is a risk factor for type 2 diabetes mellitus (T2DM) due to increased insulin resistance. In contrast, patients with a family history of T1DM are at increased risk of developing T1DM, which results from decreased insulin secretion.

(Choice E) Vaginal adenosis is the persistence of glandular columnar epithelium in the vagina and is a precursor for clear cell adenocarcinoma of the vagina. Female offspring exposed to diethylstilbestrol in utero are at increased risk and may present with vaginal discharge or vaginal cysts/fleshy colored lesions.

Educational objective:
Polycystic ovary syndrome (PCOS) is associated with oligomenorrhea, hirsutism, and polycystic ovaries. Disruption in intraovarian steroidogenesis causes anovulatory cycles and results in chronic estrogen stimulation with decreased progesterone secretion, placing PCOS patients at risk for endometrial hyperplasia/carcinoma.

References

- ACOG Practice Bulletin No. 108: Polycystic Ovary Syndrome.
- Catch It Before It Kills: Progesterone, Obesity, and the Prevention of Endometrial Cancer

Physiology	Female Reproductive System & Breast	Polycystic ovary disease
Subject	System	Topic

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A 14-year-old girl is brought to the physician for a routine checkup. When asked about her menstrual periods, she says that she does not get them every month. When she does have her period, she bleeds for 7-10 days and needs to use nearly twice as many tampons a day as her older sister. She also complains of occasional spotting that happens outside of her normal periods. The patient underwent menarche a year ago and her last period was 6 weeks ago. She eats a balanced diet and exercises 3 times a week with her volleyball team. Her past medical history is unremarkable, and her body mass index is 25 kg/m^2. Which of the following is the most likely cause of this patient's complaints?

A. Anovulatory cycles

B. Complex atypical hyperplasia of the endometrium

C. Endometrial atrophy

D. Endometrial stimulation by progesterone

E. Increased follicle-stimulating hormone secretion

Submit

A 14-year-old girl is brought to the physician for a routine checkup. When asked about her menstrual periods, she says that she does not get them every month. When she does have her period, she bleeds for 7-10 days and needs to use nearly twice as many tampons a day as her older sister. She also complains of occasional spotting that happens outside of her normal periods. The patient underwent menarche a year ago and her last period was 6 weeks ago. She eats a balanced diet and exercises 3 times a week with her volleyball team. Her past medical history is unremarkable, and her body mass index is 25 kg/m^2. Which of the following is the most likely cause of this patient's complaints?

- ✓ A. Anovulatory cycles (76%)
- B. Complex atypical hyperplasia of the endometrium (9%)
- C. Endometrial atrophy (1%)
- D. Endometrial stimulation by progesterone (5%)
- E. Increased follicle-stimulating hormone secretion (6%)

Omitted
Correct answer
A

76%
Answered correctly

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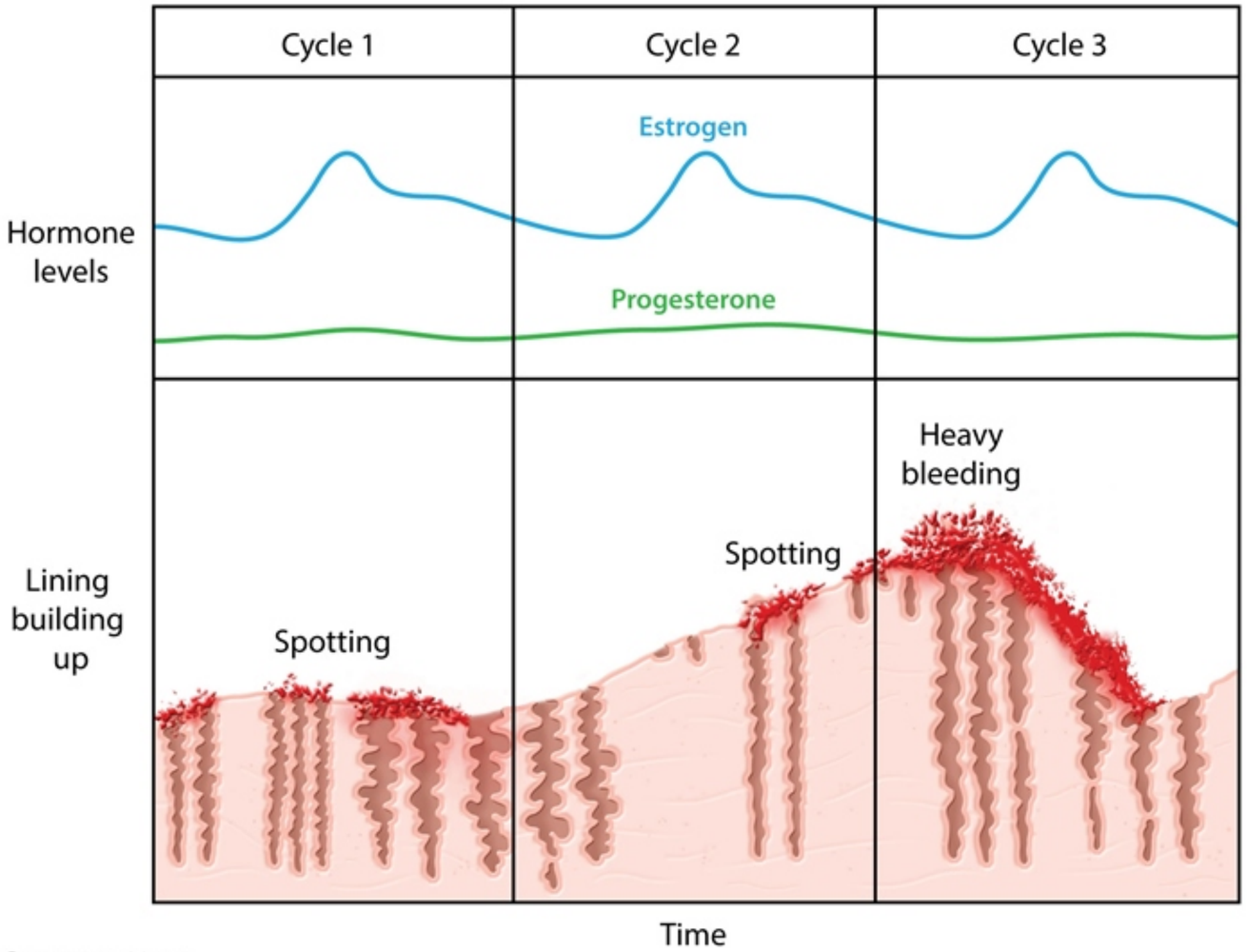
Explanation

Effects of anovulatory cycles on the endometrium

Cycle 1	Cycle 2	Cycle 3

Effects of anovulatory cycles on the endometrium



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In most women age 20-40 years, menstrual cycles are consistent and last 24-35 days, with menstrual flow ranging from 4-6 days. However, adolescents typically have an immature hypothalamic-pituitary-ovarian axis for several years following menarche. During this time, they may have longer menstrual cycles and irregular bleeding patterns due to the presence of anovulatory cycles. In the absence of ovulation, the ovarian follicle does not degenerate and become a corpus luteum. As a result, no progesterone is produced and estrogen levels remain persistently high, causing the endometrium to remain in the proliferative phase. Chronically proliferative endometrium becomes disorganized and fragile with unstable venous capillaries, resulting in irregular periods of stromal breakdown with variable, but often heavy, bleeding.

By young adulthood, ovulation occurs regularly and menstrual cycles become more predictable. However, as women approach menopause in their late 40s, anovulation becomes more prevalent and menstrual irregularity ensues.

(Choice B) Complex atypical hyperplasia of the endometrium is associated with prolonged exposure to estrogen without opposing progesterone, which may develop from chronic anovulation over many years. This condition is most common in obese older women or those who receive estrogen without progesterone during hormone replacement therapy.

(Choice C) Endometrial atrophy is an expected finding in post-menopausal women or women using certain types of hormonal contraception. Endometrial atrophy can cause intermittent spotting.

(Choice D) In a normal ovulatory cycle, estrogen stimulates endometrial proliferation and progesterone stimulates endometrial secretory changes in preparation for implantation. When estrogen and progesterone levels drop toward the end of the cycle, the loss of trophic stimulus causes the endometrium to degenerate, resulting in menstrual bleeding.

(Choice E) Increased follicle-stimulating hormone secretion occurs in post-menopausal women or in premature ovarian failure when ovaries no longer produce the estrogen that provides normal negative feedback to the pituitary gland.

Educational objective:
Anovulation is common in the first several years after menarche and the last few years before menopause. It manifests with marked menstrual cycle variability.

Physiology	Female Reproductive System & Breast	Menstrual cycles
Subject	System	Topic

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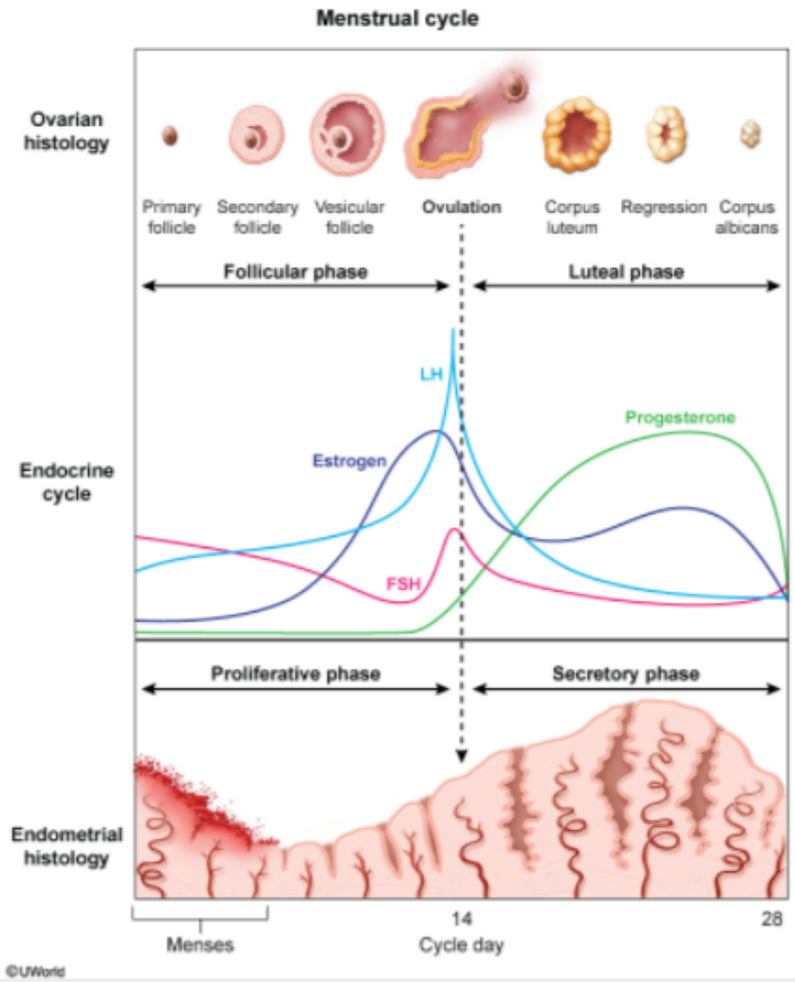

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A 23-year-old female is being evaluated for infertility. Hormone studies reveal a normal rise in the blood estradiol level during the first phase of the menstrual cycle. Androgens synthesized in this patient's ovaries are converted to estradiol in which of the following cell types?

A. Theca interna

B. Theca externa

C. Granulosa

D. Oocyte

E. Leydig

Submit

A 23-year-old female is being evaluated for infertility. Hormone studies reveal a normal rise in the blood estradiol level during the first phase of the menstrual cycle. Androgens synthesized in this patient's ovaries are converted to estradiol in which of the following cell types?

A. Theca interna (13%)

B. Theca externa (8%)

✓ C. Granulosa (72%)

D. Oocyte (1%)

E. Leydig (3%)

Omitted
Correct answer
C

72%
Answered correctly

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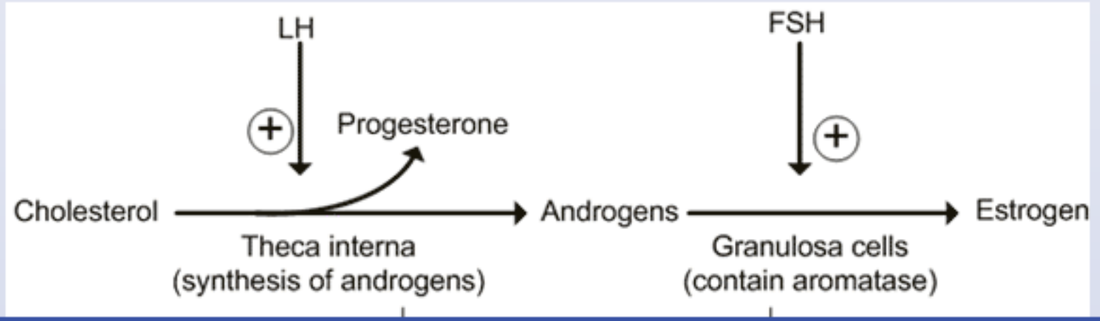
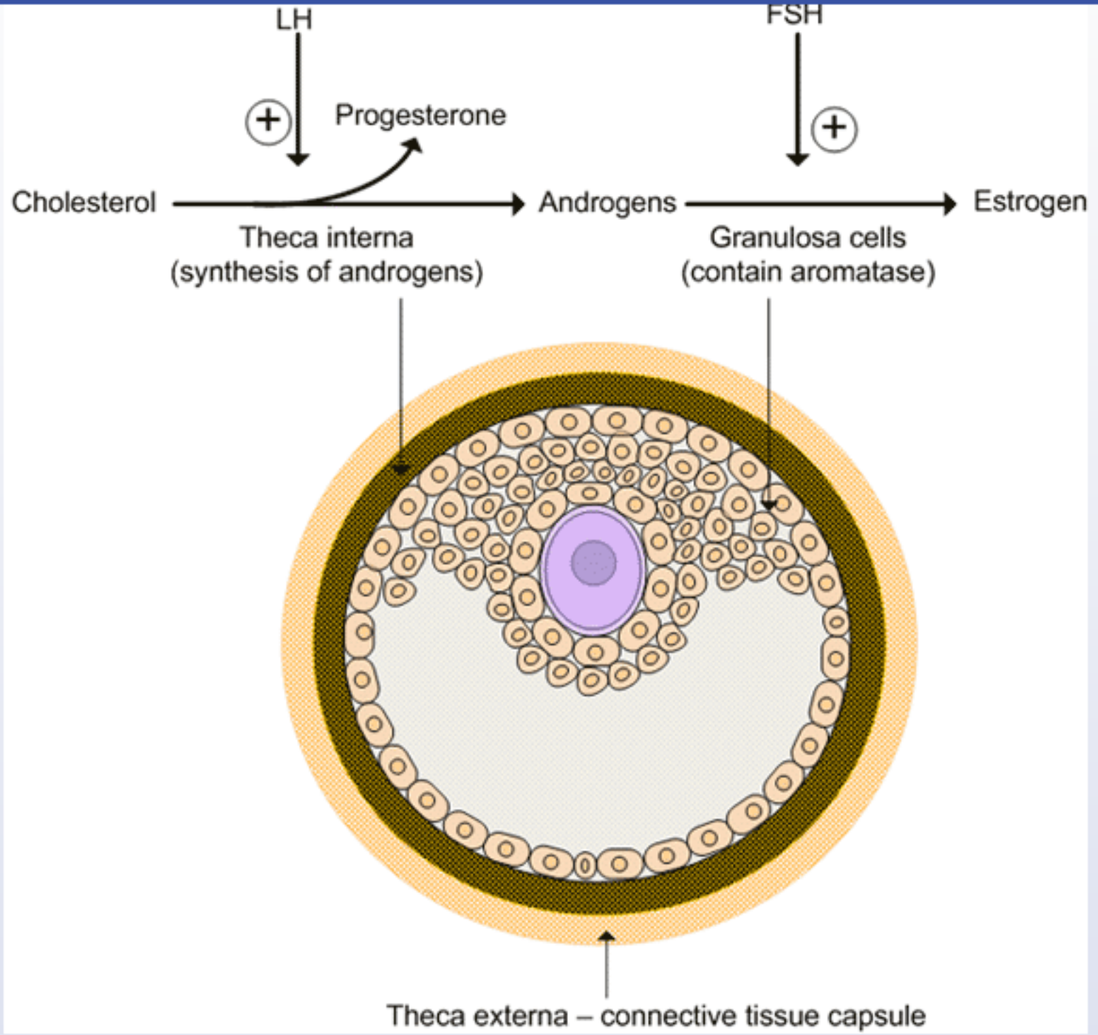
Time Spent

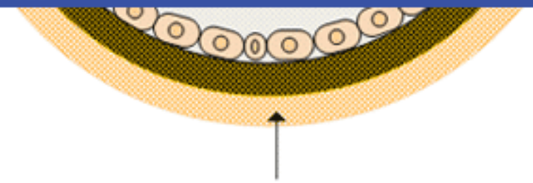
02/03/2020
Last Updated

Explanation





Estradiol, the predominant estrogen in the human body, is primarily derived from androgens. Androgens and progesterone are synthesized from cholesterol in the theca interna cells under the influence of luteinizing hormone (LH). Androgens released from the theca interna cells migrate into the nearby granulosa cells, which contain the enzyme aromatase. Aromatase converts the androgens into estradiol. This reaction is stimulated



Estradiol, the predominant estrogen in the human body, is primarily derived from androgens. Androgens and progesterone are synthesized from cholesterol in the theca interna cells under the influence of luteinizing hormone (LH). Androgens released from the theca interna cells migrate into the nearby granulosa cells, which contain the enzyme aromatase. Aromatase converts the androgens into estradiol. This reaction is stimulated by follicle stimulating hormone (FSH).

(Choice B) The theca externa lies outside of the theca interna and does not participate in steroidogenesis. The theca externa is composed of a layer of smooth muscle and fibroblast cells. It serves as a connective tissue support structure for the follicle.

(Choice D) Oocytes do not make the aromatase enzyme needed for conversion of androgens to estradiol. All female oocytes are formed during embryogenesis and remain arrested in prophase I until ovulation occurs. At each ovulation, a single oocyte completes meiosis I. Meiosis II occurs after fertilization.

(Choice E) Leydig cells are found only in the male testes. They are analogous in location and function to the theca interna cells of the ovarian follicle. Leydig cells are stimulated by LH to secrete testosterone.

Educational Objective:
LH stimulates the theca interna cells of the ovarian follicle to produce androgens. Aromatase within the follicle's granulosa cells subsequently converts these androgens to estradiol under FSH stimulation. The theca externa cells serve as a connective tissue support structure for the follicle.

Physiology	Female Reproductive System & Breast	Infertility
Subject	System	Topic

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